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(54) Title: NOVEL BACTERIAL GENES AND PROTEINS THAT ARE ESSENTIAL FOR CELL VIABILITY AND THEIR
USES

(57) Abstract: The present invention provides novel bacterial genes and their encoded polypeptides thereof which are essential for
bacterial cell viability, and their uses.

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NOVEL BACTERIAL GENES AND PROTEINS THAT ARE ESSENTIAL FOR CELL VIABILITY AND THEIR USES

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10 Throughout this application various publications are referenced. The disclosures of these publications in their entireties are hereby incorporated by reference into this application in order to more fully describe the state of the art to which this invention pertains.

FIELD OF THE INVENTION

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The present invention relates generally to nucleotide sequences, and polypeptides encoded by the sequences, that are essential for bacterial viability, and to methods of using the nucleotide and polypeptide sequences.

20 BACKGROUND OF THE INVENTION

Bacterial genera, such as *Streptococcus*, *Staphylococcus*, *Pseudomonas*, *Yersinia*, *Salmonella*, and *Enterobacter*, are the cause of numerous afflictions in humans and animals. Bacterial infection can lead to serious health conditions, including pneumonia, osteomyelitis, meningitis, sinusitis, otitis, cystitis, and even food poisoning. Typically, these infections can be treated with standard antimicrobial agents such as antibiotics. However, the emergence of pathogenic bacterial strains that are resistant to antibiotics has risen alarmingly in the past two decades. This situation has created an urgent need for the development of new antimicrobial agents.

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One strategy for developing new antimicrobial agents is to identify bacterial gene sequences that encode gene products that are essential for bacterial cell viability and

develop and/or identify agents which inhibit the function of the gene product. DNA sequencing technology has advanced from sequencing one gene at a time to sequencing entire genomes, the sum of all genes in an organism. With the recent arrival of bacterial genomic information, it is now possible to compare multiple bacterial genomes in an attempt to identify genes that encode conserved gene products. In this manner, one skilled in the art may identify a set of conserved bacterial genes, including a subset of genes that are essential for bacterial cell viability. The essential gene is then used as a starting point to develop therapeutic agents that inhibit or inactivate the product of the essential gene.

The availability of DNA sequence information for multiple microbial genomes is a recent development. The public release of the first complete genome, *Haemophilus influenzae* (Fleischmann, R.D., et al. 1995 *Science* 269:496-512), was followed in rapid succession by a number of public and private genome sequencing programs. Presently, some 20 completely sequenced bacterial genomes have been published, and over 100 other sequencing projects are underway (Blattner, F.R., et al., 1997 *Science* 277:1453-74; Ferretti, J.J., et al., 1997 *Adv Exp Med Biol* 418:961-963; Koonin, E.V., et al., 1996 *Methods Enzymol* 266:295-322). Analyses of these data indicate that approximately 46% of putative bacterial genes are of unknown function having no attributable function.

Others have pursued various strategies to identify bacterial genes that are essential for viability. These strategies include: identifying genes that are expressed by the bacteria when present in the infected host (Hensel, M., et al., 1995 *Science* 269:400-3), identifying essential genes by isolating temperature sensitive mutants (Schmid, M.B., et al., 1998 *Curr Opin Chem Biol* 2:529-34), and identifying genes in pathways known from prior physiological studies to be essential (Skarzynski, T. et al., 1996 *Structure* 1996 4:1465-74)

There continues to be a need to identify bacterial genes that encode gene products that are essential for cell viability, such as cell replication, growth, and survival. These genes and their encoded gene products can be used as a starting point towards identifying agents

that inhibit functions essential for cell viability, thereby causing bacterial cell stasis or death (e.g., antibacterial agents).

5 The present invention provides experimental identification of novel, conserved essential genes (*ceg*) from bacteria and their encoded protein products. The *ceg* genes are considered essential to cell viability because disruption of an endogenous *ceg* gene results in lethality of a bacterial cell (e.g., as determined by failure to recover viable chloramphenicol-resistant colonies, as described herein). Thus, the gene products encoded by these genes are potentially valuable targets for chemotherapeutic intervention
10 of bacterial infections.

The *ceg* nucleotide sequences of the invention were obtained by large-scale computational comparisons of multiple genome sequences to identify conserved protein coding regions, followed by gene disruption to identify *cegs*. The conservation of protein
15 sequences in many cases is believed to reflect the higher level conservation of common biochemical pathways essential for bacterial function and viability.

SUMMARY OF THE INVENTION

20 The acronyms "CEG" and "*ceg*" stand for Conserved Essential Gene. For convenience, the italicized term *ceg* refers herein to *ceg* nucleotide sequences. The capitalized term CEG refers herein to CEG polypeptide sequences.

Embodiments of the *ceg* nucleotide sequences and the CEG polypeptide sequences are
25 designated CFEs which stands for CEG For Expression. The CFEs are polypeptides resulting from expression of the *ceg* nucleotide sequence.

The present invention provides isolated nucleotide sequences of conserved essential genes from bacteria, designated *ceg*. The invention also provides recombinant nucleic
30 acid molecules including the *ceg* sequences of the invention, and methods of uses thereof. Examples of nucleic acid molecules having *ceg* sequences are described in SEQ ID

NOS.: 1-113. The invention further provides isolated polypeptides and recombinant polypeptides having the CEG sequences of the invention, and methods of uses thereof. Examples of polypeptides having CEG sequences are described in SEQ ID NOS.: 114-226.

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The *ceg* sequences of the present invention are DNA or RNA. Further, the invention includes nucleic acid molecules that are identical or nearly identical (e.g., similar) with the *ceg* sequences of the invention. The invention additionally provides polynucleotide sequences that hybridize under stringent conditions to the *ceg* sequences of the invention.

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A further embodiment provides polynucleotide sequences which are complementary to the *ceg* sequences of the invention. Yet another embodiment provides *ceg* nucleic acid molecules that are labeled with a detectable marker. Another embodiment provides recombinant nucleic acid molecules, such as a vector or a fusion molecule, including the *ceg* sequences of the invention.

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The present invention provides various *ceg* sequences, fragments thereof having essential gene activity, and related molecules such as antisense molecules, oligonucleotides, peptide nucleic acids (PNA), fragments, and portions thereof.

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The present invention relates to the inclusion of the polynucleotides encoding CEG gene products, such as CEG polypeptides, in an expression vector which can be used to transform host cells or organisms. Such transgenic hosts are useful for the production of CEG gene products for the development of antibacterial agents such as antibiotics.

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The invention further provides substantially purified CEG gene products, and uses thereof.

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The invention also relates to pharmaceutical compositions comprising antisense molecules capable of disrupting expression of *ceg* sequences, agonists, antagonists or inhibitors of CEG gene products, and antibodies reactive against the CEG polypeptides.

These compositions are useful for preventing the growth or survival of bacteria, for example, in the treatment of conditions associated with bacterial infections.

BRIEF DESCRIPTION OF THE FIGURES

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Figure 1: A schematic representation of the gene disruption assay, as described in Example 3, *infra*. A) A recombinant vector undergoing homologous recombination with the host genome. B) The result of homologous recombination.

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Figure 2: A schematic representation of the polarity test for operons, as described in Examples 2 and 3, *infra*. A) The recombinant vector undergoing homologous recombination with the host genome. B) Case 1: one possible result of homologous recombination; the downstream Gene B has an independent promoter. C) Case 2; another possible result of homologous recombination; the downstream Gene B does not have an

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Figure 3: Purification of 2CFE 75, as described in Example 6, *infra*. A) Fractionation profile of 2CFE 75 eluted from a Ni-NTA column. B) Gel electrophoresis of pooled fractions of CFE 75. C) Non-denaturing gel electrophoresis to determine oligo form of

20

Figure 4: Fractionation profile of 2CFE 3 eluted from a hydroxyapatite column, as described in Example 7, *infra*.

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Figure 5: The biosynthesis pathway of Coenzyme A which starts with phosphorylation of pantothenate.

30

Figure 6: Circular dichroism spectra of 2CFE 101 and 103, as described in Example 10, *infra*. A) Circular dichroism spectra of 2CFE 101 and 103 at 25 degrees C. B) Circular dichroism thermal melt spectra of 2CFE 101 and 103 at a range of zero to 100 degrees C.

Figure 7: Circular dichroism spectra of aggregate and monomer pools of 2CFE 101 and 103, as described in Example 10, *infra*. A) Circular dichroism spectra of aggregate and monomer pools of 2CFE 101 and 103 at 25 degrees C. B) Circular dichroism thermal melt spectra of aggregate and monomer pools of 2CFE 101 and 103 at a range of zero to 100 degrees C.

5

Figure 8: Absorbance spectra of pantothenate-dependent production of ADP, as described in Example 10, *infra*.

Figure 9: The results of size exclusion chromatography and gel electrophoresis showing the oligomeric forms of 2CFE 21 and 39, as described in Example 11, *infra*. Lanes 1-6 contain 2CFE 21, lane 7 is a molecular weight marker, lanes 8-10 contain 2CFE 39.

Figure 10: Gel electrophoresis of a helicase reaction using 2CFE 21 and 39 and radiolabeled synthetic Holliday Junction template, as described in Example 11, *infra*. Lane 1 contains the synthetic Holliday Junction template; lane 2 contains the synthetic duplex; lane 3 contains a single-stranded template; lane 4 contains the helicase reaction using 2CFE 39; lane 5 contains the helicase reaction using 2CFE 21; lanes 6-8 contain the helicase reaction using 2CFE 39 and 21 at varying concentrations (e.g., 1, 2, and 3 μ M each); and lane 9 contains the helicase reaction using 2 μ M each 2CFE 39 and 21 in the presence of ethidium bromide.

20

Figure 11: A graph depicting the results of the helicase reaction which were monitored by measuring the unquenching of the Holliday Junction templates with time, as described in Example 11, *infra*.

25

Figure 12: Capillary electrophoresis results of 2CFE 8 with and without ssDNA, as described in Example 12, *infra*. A) Electropherogram of 2CFE 8 alone. B) Electropherogram of 2CFE 8 in the presence of a 32-nucleotide single-stranded oligomer.

Figure 13: Gel mobility shift assay of 2CFE 8, and 2CFE 8 in the presence of a single-stranded 32-mer, as described in Example 12, *infra*. A) An ethidium bromide-stained,

30

native, polyacrylamide gel containing 2CFE 8, and 2CFE 8 in the presence of a 32-mer. B) The same native, polyacrylamide gel stained with Coomassie.

Figure 14: The N-acetyl glucosamine pathway putatively mediated by 2CFE 3 and 2CFE 86, as described in Example 13, *infra*.

Figure 15: Capillary electrophoresis results of 2CFE 3 with and without putative substrates, as described in Example 13, *infra*. A) Electropherogram of 2CFE 3 with and without glucosamine-1-phosphate. B) Electropherogram of 2CFE 3 with and without D-glucose-1-phosphate. C) Electropherogram of 2CFE 3 alone, 2CFE 3 and glucose-1-phosphate, and 2CFE 3 and glucose-6-phosphate. D) Electropherogram of 2CFE 3 alone or in the presence of glucosamine-1-phosphate, glucosamine-6-phosphate, D-glucose, D(+) galactose, and α -D-glucose-1-phosphate.

Figure 16: Capillary electrophoresis results of FITC-derivitized 2CFE 3 polypeptide with and without D-glucosamine-6-phosphate (substrate) to produce the product D-glucosamine-1-phosphate, using laser-induced fluorescence, as described in Example 13, *infra*. Electropherogram of D-glucosamine-6-phosphate (putative substrate), 2CFE 3 reacted with D-glucosamine-6-phosphate, and the product glucosamine-1-phosphate.

Figure 17: Gel electrophoresis of 2CFE 86 eluted from an Ni-NTA column, as described in Example 13, *infra*.

Figure 18: HPLC analysis of a coupled reaction including 2CFE 3, 2CFE 86, and D-glucosamine-6-phosphate to produce the product, UDP-N-acetylglucosamine-1-phosphate (UDPAG), as described in Example 13, *infra*.

Figure 19: A fatty acid biosynthesis pathway.

Figure 20: Size exclusion chromatography to determine the molecular weight and oligomeric form of 2CFE 34, as described in Example 14, *infra.*. Selected eluted samples were sized by gel electrophoresis.

5 Figure 21: Gel electrophoresis of 2CFE 41 eluted from a Ni-NTA column, as described in Example 15, *infra.*

Figure 22: Capillary electrophoresis results of 2CFE 40, 41, and 46, as described in Example 15, *infra.*

10

Figure 23: Depicts a schematic diagram of a ligand which binds 2CFE 34. The ligand is 2-phenyl-N-(3 carboxyl-4hydroxyphenyl) azabicyclo [4.3.0] nona-2, 8-diene.

15 Figure 24: Depicts a schematic diagram of a ligand which binds 2CFE 43. The ligand is N-(3, 5-dinitrobenzyl)-7-trifluoromethyl benza diaza furanolactone.

Figure 25: Depicts a schematic diagram of a ligand which binds 2CFE 43. The ligand is 2-amino (N-para-methylphenyl sulfonamide)-3-phenylpropionic acid.

20 Figure 26: A nucleic acid sequence of 2CFE1 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 27: A nucleic acid sequence of 2CFE2 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

25

Figure 28: A nucleic acid sequence of 2CFE3 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

30 Figure 29: A nucleic acid sequence of 2CFE4 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 30: A nucleic acid sequence of 2CFE5 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

5 Figure 31: A nucleic acid sequence of 2CFE6 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 32: A nucleic acid sequence of 2CFE7 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

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Figure 33: A nucleic acid sequence of 2CFE8 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

15 Figure 34: A nucleic acid sequence of 2CFE9 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 35: A nucleic acid sequence of 2CFE10 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

20 Figure 36: A nucleic acid sequence of 2CFE11 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 37: A nucleic acid sequence of 2CFE12 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

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Figure 38: A nucleic acid sequence of 2CFE13 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

30 Figure 39: A nucleic acid sequence of 2CFE14 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 40: A nucleic acid sequence of 2CFE15 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

5 Figure 41: A nucleic acid sequence of 2CFE16 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 42: A nucleic acid sequence of 2CFE17 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

10 Figure 43: A nucleic acid sequence of 2CFE19 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 44: A nucleic acid sequence of 2CFE21 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

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Figure 45: A nucleic acid sequence of 2CFE24 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

20 Figure 46: A nucleic acid sequence of 2CFE25 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 47: A nucleic acid sequence of 2CFE26 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

25 Figure 48: A nucleic acid sequence of 2CFE27 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 49: A nucleic acid sequence of 2CFE28 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

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Figure 50: A nucleic acid sequence of 2CFE29 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 51: A nucleic acid sequence of 2CFE30 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 52: A nucleic acid sequence of 2CFE31 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 53: A nucleic acid sequence of 2CFE32 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 54: A nucleic acid sequence of 2CFE33 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 55: A nucleic acid sequence of 2CFE34 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 56: A nucleic acid sequence of 2CFE35 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 57: A nucleic acid sequence of 2CFE36 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 58: A nucleic acid sequence of 2CFE37 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 59: A nucleic acid sequence of 2CFE38 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 60: A nucleic acid sequence of 2CFE39 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 61: A nucleic acid sequence of 2CFE40 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 62: A nucleic acid sequence of 2CFE41 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 63: A nucleic acid sequence of 2CFE42 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 64: A nucleic acid sequence of 2CFE43 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 65: A nucleic acid sequence of 2CFE44 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 66: A nucleic acid sequence of 2CFE45 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 67: A nucleic acid sequence of 2CFE46 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 68: A nucleic acid sequence of 2CFE47 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 69: A nucleic acid sequence of 2CFE48 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 70: A nucleic acid sequence of 2CFE49 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 71: A nucleic acid sequence of 2CFE50 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 72: A nucleic acid sequence of 2CFE51 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 73: A nucleic acid sequence of 2CFE52 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 74: A nucleic acid sequence of 2CFE53 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 75: A nucleic acid sequence of 2CFE54 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 76: A nucleic acid sequence of 2CFE55 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 77: A nucleic acid sequence of 2CFE56 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 78: A nucleic acid sequence of 2CFE57 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 79: A nucleic acid sequence of 2CFE58 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 80: A nucleic acid sequence of 2CFE59 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

5 Figure 81: A nucleic acid sequence of 2CFE60 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 82: A nucleic acid sequence of 2CFE61 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

10 Figure 83: A nucleic acid sequence of 2CFE62 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 84: A nucleic acid sequence of 2CFE64 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

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Figure 85: A nucleic acid sequence of 2CFE65 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

20 Figure 86: A nucleic acid sequence of 2CFE66 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 87: A nucleic acid sequence of 2CFE67 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

25 Figure 88: A nucleic acid sequence of 2CFE68 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 89: A nucleic acid sequence of 2CFE69 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

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Figure 90: A nucleic acid sequence of 2CFE70 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

5 Figure 91: A nucleic acid sequence of 2CFE71 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 92: A nucleic acid sequence of 2CFE72 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

10 Figure 93: A nucleic acid sequence of 2CFE75 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 94: A nucleic acid sequence of 2CFE76 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

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Figure 95: A nucleic acid sequence of 2CFE78 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

20 Figure 96: A nucleic acid sequence of 2CFE79 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 97: A nucleic acid sequence of 2CFE80 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

25 Figure 98: A nucleic acid sequence of 2CFE81 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 99: A nucleic acid sequence of 2CFE82 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

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Figure 100: A nucleic acid sequence of 2CFE83 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

5 Figure 101: A nucleic acid sequence of 2CFE84 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 102: A nucleic acid sequence of 2CFE85 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

10 Figure 103: A nucleic acid sequence of 2CFE86 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 104: A nucleic acid sequence of 2CFE87 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

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Figure 105: A nucleic acid sequence of 2CFE88 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

20 Figure 106: A nucleic acid sequence of 2CFE89 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 107: A nucleic acid sequence of 2CFE90 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

25 Figure 108: A nucleic acid sequence of 2CFE91 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 109: A nucleic acid sequence of 2CFE92 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

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Figure 110: A nucleic acid sequence of 2CFE94 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 111: A nucleic acid sequence of 2CFE95 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 112: A nucleic acid sequence of 2CFE96 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 113: A nucleic acid sequence of 2CFE97 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 114: A nucleic acid sequence of 2CFE99 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 115: A nucleic acid sequence of 2CFE101 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 116: A nucleic acid sequence of 2CFE102 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 117: A nucleic acid sequence of 2CFE103 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 118: A nucleic acid sequence of 2CFE104 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 119: A nucleic acid sequence of 2CFE105 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 120: A nucleic acid sequence of 2CFE106 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

5 Figure 121: A nucleic acid sequence of 2CFE107 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 122: A nucleic acid sequence of 2CFE108 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

10 Figure 123: A nucleic acid sequence of 2CFE109 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 124: A nucleic acid sequence of 2CFE111 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

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Figure 125: A nucleic acid sequence of 2CFE112 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

20 Figure 126: A nucleic acid sequence of 2CFE113 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 127: A nucleic acid sequence of 2CFE114 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

25 Figure 128: A nucleic acid sequence of 2CFE115 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 129: A nucleic acid sequence of 2CFE116 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

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Figure 130: A nucleic acid sequence of 2CFE117 deposited with the American Type Culture Collection as ATCC designation _____ on December 20, 2000.

Figure 131: Schematic structures of alkylolids which are ligands, for example, of 2CFE42.

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DETAILED DESCRIPTION OF THE INVENTION

Definitions

10 All scientific and technical terms used in this application have meanings commonly used in the art unless otherwise specified. As used in this application, the following words or phrases have the meanings specified.

As used herein, a *ceg* nucleic acid molecule is said to be "isolated" when the nucleic acid
15 molecule is substantially separated from contaminant nucleic acid molecules that encode polypeptides other than CEGs. Additionally, isolated nucleic acid molecule refers to any RNA or DNA sequence obtained from a natural source, or constructed by recombinant methods, or synthesized. A skilled artisan can readily employ nucleic acid isolation procedures to obtain an isolated nucleic acid molecule having *ceg* sequences.

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The term "*ceg*" includes all isolated forms of *ceg* nucleotide and CEG amino acid sequences disclosed herein. The *ceg* sequences encode gene products that have essential biological functions in bacterial cells, such as, for example, nucleotide biosynthesis, amino acid biosynthesis, DNA replication, RNA transcription, protein translation, DNA
25 recombination, DNA repair, biosynthesis of cofactors (e.g., Coenzyme A), biosynthesis of prosthetic groups, cellular processes (e.g., chaperones, cell division, and polypeptide secretion), energy metabolism (e.g., pentose phosphate pathway, glycolysis, gluconeogenesis), fatty acid biosynthesis, cell wall biosynthesis, and/or biosynthesis of purines, pyrimidines, nucleosides, and nucleotides. Accordingly, the gene products of the
30 *ceg* nucleotide sequences are required for viability of bacterial cells. The term "*ceg*" also includes variants having nucleotide sequence similarity to the disclosed *ceg* sequences,

including sequences isolated from various bacterial genera and species, allelic variants, mutant variants, and *ceg* variants that encode conservative and non-conservative amino acid substitutions. The present invention also provides for all *ceg* sequences generated by recombinant DNA technology, including complementary sequences, *ceg* sequences that
5 hybridize to the sequences of the invention at high stringency hybridization conditions, fusion genes comprising a *ceg* sequence, and codon usage variants.

The term "essential genes" refers to a nucleotide sequence that encodes a gene product having a function which is required for cell viability. The term "essential protein" refers
10 to a polypeptide that is encoded by an essential gene and has a function that is required for cell viability. Accordingly, a mutation that disrupts the function of the essential gene or essential proteins results in a loss of viability of cells harboring the mutation.

"Non-essential genes" or "non-essential proteins" refer to genomic information, or the
15 protein(s) or RNAs encoded therefrom which, when disrupted by a mutation, do not result in a loss of viability of cells harboring said mutation under defined laboratory conditions.

As used herein, a nucleotide sequence is said to be "identical" to another reference
20 sequence when both nucleotide sequences are exactly alike.

As used herein, a nucleotide sequence is said to be "similar" to another reference sequence when a comparison of the two sequences shows that they have a low level of sequence differences. For example, two sequences are considered to be similar to each
25 other when the percentage of nucleotides that are shared between the two sequences is between about 70 % to 99.99% over the entire length of the two sequences.

As used herein an amino acid sequence is said to be "similar" to another reference sequence when a comparison of the two sequences shows that they have a low level of
30 sequence differences. For example, two sequences are considered to be similar to each

other when the percentage of amino acids that are shared between the two sequences may be between about 30% to 100% identity over the entire length of the two sequences.

As used herein, an "allele" or "allelic sequence" is an alternative form of the naturally-occurring *ceg* sequence. Alleles result from a mutation, that changes the nucleotide sequence, and generally produce altered mRNAs or polypeptides whose structure or function may or may not be altered.

"Substantially purified" as used herein means a specific isolated nucleic acid or protein, or fragment thereof, in which substantially all contaminants (i.e. substances that differ from said specific molecule) have been separated from said nucleic acid or protein.

In a host cell, an "endogenous" sequence as used herein means a nucleic acid sequence that is naturally-occurring and resides within the host genome.

In a host cell, an "exogenous" sequence as used herein means an isolated nucleic acid sequence that is introduced into the host cell, using any one of a variety of introduction methods, such as transfection, electroporation, cationic lipid or salt treatment methods.

"Knockout mutant" or "knockout mutation" as used herein refers to an *in vitro* engineered disruption of a region of endogenous chromosomal DNA (e.g., disruption of the genome), typically within a protein coding region. A knockout mutation can be generated by inserting an exogenous DNA sequence into the homologous endogenous sequence. A knockout mutation occurring in a protein coding region is expected to disrupt normal expression of the protein coding region. This usually leads to loss of the function provided by the protein.

In order that the invention herein described may be more fully understood, the following description is set forth.

A) MOLECULES OF THE INVENTION

1.) CEG NUCLEIC ACID MOLECULES

- 5 The present invention provides isolated and recombinant *ceg* nucleic acid molecules and fragments thereof, and related molecules, such as sequences complementary to *ceg* sequences or a portion thereof, and those that hybridize to the nucleic acid molecules of the invention.
- 10 The *ceg* polynucleotide sequences, also referred to herein as nucleic acid molecules of the invention, are preferably in isolated form, including DNA, RNA, DNA/RNA hybrids, and related molecules, and fragments thereof. Specifically contemplated are genomic DNA, ribozymes, and antisense molecules, as well as nucleic acid molecules based on an alternative backbone or including alternative bases, whether derived from natural sources or
- 15 synthesized. Embodiments of particular *ceg* polynucleotide and amino acid sequences include, but are not limited to, the sequences described in Tables I and II (e.g., SEQ ID NOS:1-113, 114-226 and SEQ ID NOS: 227-339, 340-452, respectively). The *ceg* polynucleotide and amino acid sequences were designated *cef* which stands for CEG For Expression.

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Biological samples of the 2CFE nucleic acid molecules (e.g., SEQ ID NOS: 227-331) were deposited on December 20, 2000 with the American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, VA 20110-2209.

TABLE I

CFE Designation	SEQ. ID NO. (Nucleotide)	SEQ. ID NO. (Polypeptide)	POLARITY
CFE 1	1	114	+
CFE 2	2	115	-
CFE 3	3	116	-
CFE 4	4	117	+
CFE 5	5	118	-
CFE 6	6	119	+

TABLE I

CFE Designation	SEQ. ID NO. (Nucleotide)	SEQ. ID NO. (Polypeptide)	POLARITY
CFE 7	7	120	-
CFE 8	8	121	+
CFE 9	9	122	+
CFE 10	10	123	+
CFE 11	11	124	+
CFE 12	12	125	+
CFE 13	13	126	-
CFE 14	14	127	+
CFE 15	15	128	-
CFE 16	16	129	-
CFE 17	17	130	-
CFE 19	18	131	+
CFE 21	19	132	-
CFE 24	20	133	-
CFE 25	21	134	+
CFE 26	22	135	-
CFE 27	23	136	+
CFE 28	24	137	-
CFE 29	25	138	-
CFE 30	26	139	-
CFE 31	27	140	+
CFE 32	28	141	+
CFE 33	29	142	-
CFE 34	30	143	+
CFE 35	31	144	+
CFE 36	32	145	+
CFE 37	33	146	-
CFE 38	34	147	+
CFE 39	35	148	-
CFE 40	36	149	-
CFE 41	37	150	-
CFE 42	38	151	-
CFE 43	39	152	-
CFE 44	40	153	+
CFE 45	41	154	-
CFE 46	42	155	-

TABLE I

CFE Designation	SEQ. ID NO. (Nucleotide)	SEQ. ID NO. (Polypeptide)	POLARITY
CFE 47	43	156	-
CFE 48	44	157	
CFE 49	45	158	+
CFE 50	46	159	+
CFE 51	47	160	+
CFE 52	48	161	-
CFE 53	49	162	+
CFE 54	50	163	+
CFE 55	51	164	+
CFE 56	52	165	+
CFE 57	53	166	+
CFE 58	54	167	+
CFE 59	55	168	-
CFE 60	56	169	+
CFE 61	57	170	+
CFE 62	58	171	
CFE 63	59	172	
CFE 64	60	173	+
CFE 65	61	174	+
CFE 66	62	175	+
CFE 67	63	176	+
CFE 68	64	177	-
CFE 69	65	178	+
CFE 70	66	179	+
CFE 71	67	180	-
CFE 72	68	181	-
CFE 73	69	182	+
CFE 74	70	183	-
CFE 75	71	184	-
CFE 76	72	185	+
CFE 77	73	186	
CFE 78	74	187	+
CFE 79	75	188	-
CFE 80	76	189	-
CFE 81	77	190	+
CFE 82	78	191	

TABLE I

CFE Designation	SEQ. ID NO. (Nucleotide)	SEQ. ID NO. (Polypeptide)	POLARITY
CFE 83	79	192	-
CFE 84	80	193	-
CFE 85	81	194	-
CFE 86	82	195	-
CFE 87	83	196	-
CFE 88	84	197	-
CFE 89	85	198	+
CFE 90	86	199	+
CFE 91	87	200	-
CFE 92	88	201	-
CFE 93	89	202	+
CFE 94	90	203	+
CFE 95	91	204	+
CFE 96	92	205	+
CFE 97	93	206	-
CFE 98	94	207	
CFE 99	95	208	+
CFE 100	96	209	
CFE 101	97	210	-
CFE 102	98	211	+
CFE 103	99	212	-
CFE 104	100	213	+
CFE 105	101	214	-
CFE 106	102	215	-
CFE 107	103	216	-
CFE 108	104	217	+
CFE 109	105	218	-
CFE110	106	219	-
CFE 111	107	220	-
CFE 112	108	221	-
CFE 113	109	222	-
CFE 114	110	223	-
CFE 115	111	224	-
CFE 116	112	225	-
CFE 117	113	226	-

TABLE II

CFE Designation	SEQ. ID NO. (Nucleotide)	SEQ. ID NO. (Polypeptide)	FIGURE
2CFE 1			26
2CFE 2			27
2CFE 3			28
2CFE 4			29
2CFE 5			30
2CFE 6			31
2CFE 7			32
2CFE 8			33
2CFE 9			34
2CFE 10			35
2CFE 11			36
2CFE 12			37
2CFE 13			38
2CFE 14			39
2CFE 15			40
2CFE 16			41
2CFE 17			42
2CFE 19			43
2CFE 21			44
2CFE 24			45
2CFE 25			46
2CFE 26			47
2CFE 27			48
2CFE 28			49
2CFE 29			50
2CFE 30			51
2CFE 31			52
2CFE 32			53
2CFE 33			54
2CFE 34			55
2CFE 35			56
2CFE 36			57
2CFE 37			58
2CFE 38			59
2CFE 39			60

CFE Designation	SEQ. ID NO. (Nucleotide)	SEQ. ID NO. (Polypeptide)	FIGURE
2CFE 40			61
2CFE 41			62
2CFE 42			63
2CFE 43			64
2CFE 44			65
2CFE 45			66
2CFE 46			67
2CFE 47			68
2CFE 48			69
2CFE 49			70
2CFE 50			71
2CFE 51			72
2CFE 52			73
2CFE 53			74
2CFE 54			75
2CFE 55			76
2CFE 56			77
2CFE 57			78
2CFE 58			79
2CFE 59			80
2CFE 60			81
2CFE 61			82
2CFE 62			83
2CFE 64			84
2CFE 65			85
2CFE 66			86
2CFE 67			87
2CFE 68			88
2CFE 69			89
2CFE 70			90
2CFE 71			91
2CFE 72			92
2CFE 75			93
2CFE 76			94
2CFE 78			95
2CFE 79			96
2CFE 80			97

CFE Designation	SEQ. ID NO. (Nucleotide)	SEQ. ID NO. (Polypeptide)	FIGURE
2CFE 81			98
2CFE 82			99
2CFE 83			100
2CFE 84			101
2CFE 85			102
2CFE 86			103
2CFE 87			104
2CFE 88			105
2CFE 89			106
2CFE 90			107
2CFE 91			108
2CFE 92			109
2CFE 94			110
2CFE 95			111
2CFE 96			112
2CFE 97			113
2CFE 99			114
2CFE 101			115
2CFE 102			116
2CFE 103			117
2CFE 104			118
2CFE 105			119
2CFE 106			120
2CFE 107			121
2CFE 108			122
2CFE 109			123
2CFE 111			124
2CFE 112			125
2CFE 113			126
2CFE 114			127
2CFE 115			128
2CFE 116			129
2CFE 117			130

a) Variant *ceg* Nucleotide Sequences

The present invention also provides nucleic acid molecules having a nucleotide sequence
5 substantially identical or similar to the *ceg* sequences (SEQ ID NOS: 1-113, 227-331)
disclosed herein.

The present invention provides nucleotide sequences which are similar to SEQ ID
NOS:1-113 and/or SEQ ID NOS:227-331. The present invention provides nucleotide
10 sequences which vary from SEQ ID NOS:1-113 or 227-331 by a range of about 1% to
about 70%.

The present invention encompasses variations in polynucleotide sequences resulting from
mutations and/or from transfer of genetic material from one cell to another (e.g.,
15 horizontal gene transfer or horizontal gene exchange).

The present invention also provides for variants of the polynucleotide *ceg* sequences
disclosed herein, including variants isolated from naturally-occurring sources, those
generated by recombinant DNA technology or other in vitro synthesis methodologies
20 (e.g., PCR). The variant polynucleotide sequences of the invention encode polypeptides
that exhibit the biological activity of naturally-occurring CEG polypeptides, such as
activity required for bacterial cell viability.

In general, for example, a variant of *ceg* polynucleotide sequences may encode a
25 polypeptide that differs by one or more amino acid substitutions. The variant may have
conservative changes, wherein a substituted amino acid has similar structural or chemical
properties, eg, replacement of leucine with isoleucine.

A polynucleotide sequence can encode conservative amino acid substitutions without
30 altering either the conformation or the function of the polypeptide. Such changes include
substituting any of isoleucine (I), valine (V), and leucine (L) for any other of these

hydrophobic amino acids; aspartic acid (D) for glutamic acid (E) and vice versa; glutamine (Q) for asparagine (N) and vice versa; and serine (S) for threonine (T) and vice versa. Other substitutions can also be considered conservative, depending on the environment of the particular amino acid and its role in the three-dimensional structure of the protein. For example, glycine (G) and alanine (A) can frequently be interchangeable, as can alanine (A) and valine (V). Methionine (M), which is relatively hydrophobic, can frequently be interchanged with leucine and isoleucine, and sometimes with valine. Lysine (K) and arginine (R) are frequently interchangeable in locations in which the significant feature of the amino acid residue is its charge and the differing pK's of these two amino acid residues are not significant. Still other changes can be considered "conservative" in particular environments.

A variant may also have nonconservative changes, eg, replacement of a glycine with a tryptophan. Other variations may also include amino acid deletions or insertions, or both. Guidance in determining which and how many amino acid residues may be substituted, inserted or deleted without abolishing biological or immunological activity may be found using computer programs well known in the art, for example, DNASTAR software.

Another type of *ceg* sequence variant includes naturally-occurring allelic variants of *ceg* which share significant similarity (e.g., between about 30- 99%) to the disclosed CEG polypeptide sequence. Allelic variants of the *ceg* sequences can encode conservative or non-conservative amino acid substitutions of the CEG polypeptide sequence herein described.

An example of allelic variants of *ceg* are mutant alleles of *ceg* polynucleotide sequences that encode a polypeptide having one or more changes in the polypeptide sequence, such as amino acid substitutions, deletions, insertions, frame shifts, or truncations. The mutant alleles of *ceg* may or may not encode a CEG polypeptide having the same biological functions as wild-type CEG proteins.

Variations in the bacterial genomic sequences can also arise from transfer of genetic material to another bacterial cell. The transfer of gene sequences can occur intraspecies or interspecies. Gene transfer can occur between bacterial cells which are members of the same or different populations. A population includes, but is not limited to, a serotype isolate, a clinical isolate, a naturally-occurring isolate, a strain, and a species. The transfer of genetic material can occur between cells within a population; for example transfer between serotype A to serotype A, or between *S. pneumoniae* and *S. pneumoniae*. The transfer of genetic material can occur between cells of different populations; for example, between serotype A to serotype B or *S. pneumoniae* and *S. mutans*.

Gene transfer can give rise to mutant or polymorphic variant genes sequences. In rare cases, gene transfer introduces new gene sequences that confer a new phenotype, such as antibiotic resistance. The transfer of genetic material includes transfer of large regions of genomic sequences which include partial gene sequences, whole single gene sequences, or multiple gene sequences. This mode of transfer can give rise to replacement of native whole gene sequences or introduction of new sequences in the recipient cell. This mode of transfer gives rise to mosaic gene sequences in the recipient cell.

The variation of genomic sequences resulting from gene transfer can be examined using molecular techniques, including: multilocus enzyme electrophoresis (Selander, R. K., et al., 1986 *Appl. Environ. Microbiol.* 51:837-884); and restriction endonuclease cleavage electrophoretic profiling (Coffey, T. J., et al., 1991 *Mol. Microbio.* 5:2255-2260); pulse-field gel electrophoresis fingerprinting (Bygraves, J. A. and Maiden, M. C. J. 1992 *J. Gen. Microbiol.* 138:523-531); and ribotyping (Stull, T. L., et al., 1988 *J. Infect. Dis.* 157:280-286). The degree of variation can vary greatly, and ranges from little or no variation as exemplified by gene sequences of *E. coli* (Caugant, d. A., et al., 1981 *Genetics* 98:467-490; Whittam, T. S., et al., 1983 *Mol. Biol. Evol.* 1:67-83; Souza, V., et al., 1992 *Proc. Natl. Acad. Sci. USA* 89:8389-8393) and *Salmonella* (Selander, R. K., et al., 1990 *Infect. Immun.* 58:2262-2275; Selander, R.K. and Smith, N. H. 1990 *Rev. Med. Microbiol.* 1:219-228; Smith, J. M., et al., 1993 *Proc. Natl. Acad. Sci. USA* 90:4384-

4388), to extensive gene transfer in *Neisseria gonorrhoeae* (Smith, J. M., et al., 1993 *Proc. Natl. Acad. Sci. USA* 90:4384-4388).

Gene transfer can be examined between various isolates of a particular microbial species
5 which are antibiotic-sensitive or antibiotic-resistant (Coffey, T. J., et al., 1991 *Molec. Microbiol.* 5:2255-2260). Molecular biology techniques can be utilized to study the degree of transfer between populations, such as, for example, the degree of gene transfer between serotypes, isolates, strains, or species. The degree of transfer can be examined by comparing, for example, the penicillin binding proteins and numerous different loci
10 which encode metabolic enzymes or capsular biosynthesis enzymes.

For example, intra-species, inter-serotype, gene transfer is possible (Coffey, T. J., et al., 1991 *supra*). Additionally, intraspecies gene transfer in *S. pneumoniae* (Coffey, T. J., et al., 1998 *Mol. Microbiol.* 27:73-83), *Vibrio cholerae* (Bik, E. M., et al., 1995 *EMBO J.*
15 14:209-216), and *Haemophilus influenzae* (Kroll, J. S. and Moxon, E. R. 1990 *J. Bacteriol.* 172: 1374-1379) are possible.

Interspecies gene transfer is also possible (Dowson, C. G., et al., 1989 *Proc. Natl. Acad. Sci. USA* 86:8842-8846; Laibl, G., et al., 1991 *Mol. Microbiol.* 5:1993-2002; Bourgoin,
20 F., et al., 1999 *Gene* 233:151-161).

Variant gene sequences arising from gene transfer can be continually generated in transformable bacteria (e.g., transformation competent), such as *S. pneumoniae*. For example, the worldwide spread of varying degrees of antibiotic resistance has been
25 documented and reviewed (Dowson, C. G., et al., 1994 *Trends Microbiol.* 2:361-366; Spratt, B. G. in *Bacterial Cell Wall*, eds Ghuyssen J-M. and Hakenbeck, R. 1994 pp. 517-534; and reviewed in Maiden, M. C. J. 1998 *Clinic. Infect. Dis.* 27 (Supplement 1) S12-S20). For example, variant gene sequence arising from gene transfer can be tracked using a marker gene such as the gene which encodes the penicillin binding protein
30 (Barcus, V. A., et al., 1995 *FEMS Microbiol. Lett.* 126:299-303). At the nucleotide level, gene sequences encoding the penicillin binding proteins in susceptible and resistant

strains differ by about 14% to 23% (Hakenbeck, R. 1995 *Biochem. Pharmacol.* 50:1121-1127; Spratt, B. G. in *Bacterial Cell Wall*, eds Ghuysen J-M. and Hakenbeck, R. 1994 pp. 517-534; Spratt, B. G., et al., 1991 *Neisseria meningitidis* and *Streptococcus pneumoniae* eds. Camisi, J., et al., pp. 73-83; Coffey, T. J., et al., 1995 *Micro. Drug Resist.* 1:29-34).

5

The *ceg* nucleotide sequences can be isolated from various species of *Streptococcus* including *Streptococcus pneumoniae*. Additionally, the *ceg* sequences can be isolated from other Streptococcal species, including *S. mutans*, *S. pyogenes*, and *S. thermophila*. The *ceg* polynucleotide sequences can also be isolated from strains of other bacterial genera including, but not limited to, *Streptococcus*, *Escherichia*, *Bacillus*, *Pseudomonas*, *Yersinia*, *Salmonella*, and *Haemophilus*.

The present invention additionally provides isolated codon-usage variants that differ from the disclosed *ceg* nucleotide sequences, yet do not alter the predicted CEG polypeptide sequence or function. The codon-usage variants may be generated by recombinant DNA technology. Codons may be selected to optimize the level of production of the *ceg* transcript or CEG polypeptide in a particular prokaryotic or eukaryotic expression host, in accordance with the frequency of codon utilized by the host cell. Alternative reasons for altering the nucleotide sequence encoding a CEG polypeptide include the production of RNA transcripts having more desirable properties, such as an extended half-life or increased stability. A multitude of variant *ceg* nucleotide sequences that encode the respective CEG polypeptide may be isolated, as a result of the degeneracy of the genetic code. Accordingly, the present invention contemplates selecting every possible triplet codon to generate every possible combination of nucleotide sequences that encode the disclosed CEG polypeptides. This particular embodiment provides isolated nucleotide sequences that vary from the sequences as described in SEQ ID NOs.: 1-113 or 227-331, such that each variant nucleotide sequence encodes a polypeptide having sequence identity with the amino acid sequences, as described in SEQ ID NOs.: 114-226 or 332-436, respectively.

30

b) Complementary Sequences

The present invention includes polynucleotide sequences that are complementary to the sequences disclosed herein. The term "complementary" as used herein refers to the capacity of purine and/or pyrimidine nucleotides to associate through hydrogen bonding to form double stranded nucleic acid molecules. The following base pairs are related by complementarity: guanine and cytosine; adenine and thymine; and adenine and uracil. Complementary applies to all base pairs comprising at least two single-stranded nucleic acid molecules.

c) Sequences Capable of Hybridizing

Another embodiment provides nucleic acid molecules that will hybridize to *ceg* sequences under hybridization conditions. It is readily apparent to one skilled in the art that the stringency of the hybridization condition selected will depend upon the characteristics of the nucleic acid molecule to be hybridized, such as, the length, the degree of complementarity (e.g., exact or non-exact complementarity), the percent A/T content, and the objective of the hybridization experiment.

20

The hybridization procedure may be performed in low stringency hybridization conditions. Low stringency hybridization conditions will permit hybridization between two nucleic acid molecules that differ from exact complementarity by about 25% to 70%. Hybridization under standard high stringency conditions will occur between two complementary nucleic acid molecules (e.g., 100% exact complementarity) or two complementary nucleic acid molecules that differ from exact complementarity by about 1% to about 70%.

25

The high stringency hybridization conditions that disfavor non-homologous base pairing are well known in the art. Typically, high stringency hybridization conditions, includes but is not limited to, hybridizing at 50 °C to 65 °C in 5X SSPE, and washing at 50 °C to

30

65 °C in 0.5X SSPE. Typically, low stringency conditions, includes but is not limited to, hybridizing at 35 °C to 37 °C in 5X SSPE and 40% to 45% formamide and washing at 42 °C in 1-2X SSPE. The conditions and formulas for high stringency hybridization methods are well known in the art and can be readily obtained in *Molecular Cloning; A Laboratory Manual* (2nd edition, Sambrook, Fritsch, and Maniatis 1989, Cold Spring Harbor Press) or in *Short Protocols in Molecular Biology* (Ausubel, F. M., et al., 1989, John Wiley & Sons).

d) Fragments of *ceg* Sequences

The invention further provides nucleic acid molecules having fragments of the *ceg* sequences, such as a portion of the *ceg* sequence (e.g., SEQ ID NOS:1-113, 227-331) disclosed herein. The size of the fragment will be determined by its intended use. For example, the length of the fragment to be used as a nucleic acid probe or PCR primer is chosen to obtain a relatively small number of false positives during probing or priming. Alternatively, a fragment of the *ceg* sequence may be used to construct a recombinant fusion gene having a *ceg* sequence fused to a non-*ceg* sequence.

The nucleic acid molecules, fragments thereof, and probes and primers of the present invention are useful for a variety of molecular biology techniques including, for example, hybridization screens of libraries, or detection and quantification of mRNA transcripts as a means for analysis of gene transcription and/or expression. Preferably, the probes and primers are DNA. A probe or primer length of at least 15 base pairs is suggested by theoretical and practical considerations (Wallace, B. and Miyada, G. 1987 "Oligonucleotide Probes for the Screening of Recombinant DNA Libraries" in: *Methods in Enzymology*, 152:432-442, Academic Press). Other lengths of fragments, probes, or primers are possible and routine to determine.

The probes and primers of this invention can be prepared by methods well known to those skilled in the art (Sambrook, et al. *supra*). In a preferred embodiment the probes

and primers are synthesized by chemical synthesis methods (ed: Gait, M. J. 1984 *Oligonucleotide Synthesis*, IRL Press, Oxford, England).

One embodiment of the present invention provides nucleic acid primers that are complementary to *ceg* sequences, which allow the specific amplification of nucleic acid molecules of the invention or of any specific parts thereof. Another embodiment provides nucleic acid probes that are complementary for selectively or specifically hybridizing to the *ceg* sequences or to any part thereof.

e) Derivative Nucleic Acid Molecules

The nucleic acid molecules of the invention include peptide nucleic acids (PNAs), or derivative molecules such as phosphorothioate, phosphotriester, phosphoramidate, and methylphosphonate, that specifically bind to single-stranded DNA or RNA in a base pair-dependent manner (Zamecnik, P. C., et al., 1978 *Proc. Natl. Acad. Sci.* 75:280284; Goodchild, P. C., et al., 1986 *Proc. Natl. Acad. Sci.* 83:4143-4146).

PNA molecules comprise a nucleic acid oligomer to which an amino acid residue, such as lysine, and an amino group have been added. These small molecules, also designated anti-gene agents, stop transcript elongation by binding to their complementary (template) strand of nucleic acid (Nielsen, P. E., et al., 1993 *Anticancer Drug Des* 8:53-63). For example, reviews of methods for synthesis of DNA, RNA, and their analogues can be found in: *Oligonucleotides and Analogues*, eds. F. Eckstein, 1991, IRL Press, New York; *Oligonucleotide Synthesis*, ed. M. J. Gait, 1984, IRL Press, Oxford, England. Additionally, methods for antisense RNA technology are described in U. S. patents 5,194,428 and 5,110,802. A skilled artisan can readily obtain these classes of nucleic acid molecules using the herein described *ceg* polynucleotide sequences, see for example *Innovative and Perspectives in Solid Phase Synthesis* (1992) Egholm, et al. pp 325-328 or U. S. Patent No. 5,539,082.

f) RNA Molecules

The present invention provides RNA molecules that encode the predicted *ceg* gene products. In particular, the RNA molecules of the invention may be isolated full-length or partial mRNA molecules or RNA oligomers that encode CEG gene products. The RNA molecules of the invention include the nucleotide sequences encoding all or portions of CEGs.

The RNA molecules of the invention also include antisense RNA molecules, peptide nucleic acids (PNAs), or non-nucleic acid molecules such as phosphorothioate derivatives, that specifically bind to the sense strand of DNA or RNA in a base pair-dependent manner. A skilled artisan can readily obtain these classes of nucleic acid molecules using the herein described *ceg* sequences.

g) Labeled Nucleic Acid Molecules

The nucleic acid molecules having *ceg* sequences can be labeled with a detectable marker. Examples of a detectable marker include, but are not limited to, a radioisotope, a fluorescent compound, a bioluminescent compound, a chemiluminescent compound, a metal chelator or an enzyme. Technologies for generating labeled DNA and RNA probes are well known in the art (See e.g. Sambrook et al., *supra*).

2.) RECOMBINANT NUCLEIC ACID MOLECULES

Also provided are recombinant nucleic acid molecules, such as recombinant DNA molecules (rDNAs) that comprise *ceg* sequences or fragments thereof. As used herein, a recombinant DNA molecule is a DNA molecule that has been subjected to molecular manipulation *in vitro*. Methods for generating rDNA molecules are well known in the art, for example, see Sambrook et al., *Molecular Cloning* (1989), *supra*.

a) Vectors

The nucleic acid molecules of the invention may be recombinant molecules each comprising the sequence, or portions thereof, of a *ceg* sequence linked to a non-*ceg* sequence. For example, the *ceg* sequence may be fused operatively to a vector to generate a recombinant molecule. The term vector includes, but is not limited to, plasmids, cosmids, and phagemids. A preferred vector includes an autonomously replicating vector comprising a replicon that directs the replication of the rDNA within the appropriate host cell. The preferred vectors can also include an expression control element, such as a promoter sequence, which enables transcription of the inserted *ceg* sequences and can be used for regulating the expression (e.g., transcription and/or translation) of an operably linked *ceg* sequence in an appropriate host cell such as *Escherichia coli*. Expression control elements are known in the art and include, but are not limited to, inducible promoters, constitutive promoters, secretion signals, enhancers, transcription terminators, and other transcriptional regulatory elements. Other expression control elements that are involved in translation are known in the art, and include the Shine-Dalgarno sequence, and initiation and termination codons. The preferred vector also includes at least one selectable marker gene that encodes a gene product that confers drug resistance such as resistance to ampicillin or tetracycline. The vector also comprises multiple endonuclease restriction sites that enable convenient insertion of exogenous DNA sequences.

The preferred vectors for generating *ceg* transcripts and/or the encoded CEG polypeptides are expression vectors which are compatible with prokaryotic host cells. Prokaryotic cell expression vectors are well known in the art and are available from several commercial sources. For example, a pET vectors (e.g., pET-21, Novagen Corp.) may be used to express CEG polypeptides in bacterial host cells.

b) Recombinant Vectors for Integration

The present invention provides recombinant vectors that may be used to integrate
5 exogenously provided sequences into the genome of a host cell. The recombinant
integration vectors of the present invention include a gene that encodes a selectable
marker and *ceg* sequences, or fragments thereof. The integration vectors are used to
integrate the *ceg* sequence into a target gene sequence that resides within the bacterial
10 host genome (e.g., endogenous sequence), thereby disrupting the function of the target
gene sequence within the bacterial cells. These integration vectors may be used in a gene
disruption assay to screen candidate *ceg* nucleotide sequences, in order to identify the
candidate sequences that encode a gene product that is required for bacterial cell viability.

Accordingly, these recombinant integration vectors include candidate *ceg* sequences that
15 will be screened to determine if the candidate *ceg* sequences encode a gene product that
is required for cell viability. The candidate *ceg* sequence that is included as part of the
recombinant integration vector is the "exogenous" *ceg* sequence that is employed as the
"disrupting" sequence in a gene disruption assay. The *ceg* sequence that resides within
the host genome is the "endogenous" or "target" *ceg* sequence.

20

The integration event rarely occurs, for example, by non-homologous recombination in
which a recombinant vector, that includes the exogenous *ceg* sequence, inserts the
exogenous *ceg* sequence into a random location within the host genome. In a more
preferred embodiment, the integration event inserts the exogenous *ceg* sequence into a
25 specific target site within the host genome. The targeted integration event can involve
homologous recombination in which the integration vector, that includes the exogenous
ceg sequence, inserts the exogenous *ceg* sequence into its homologous target *ceg*
sequence that resides within the host's genome (e.g., the endogenous *ceg* sequence)
(Figure 1). Further, the exogenous *ceg* sequence can be used as a disrupting sequence
30 whereby the homologous recombination event integrates the exogenous *ceg* sequence
into the endogenous target *ceg* sequence resulting in disruption of the function of the

endogenous *ceg* sequence. For example, disrupting the function of the endogenous *ceg* sequence may result in the loss of bacterial cell viability.

5 An example of a recombinant vector that can be used as an integration vector in *S. pneumoniae* is the pEVP-3 vector (Jean-Pierre Claverys, et al. 1995 *Gene* 164: 123-128). The pEVP-3 vector integrates an exogenous sequence by homologous recombination involving a Campbell-type event (S. Adhya and A. Campbell 1970 *J. Mol. Biol.* 50:481-490). The pEVP-3 vector includes a replicon that functions only in gram-negative bacteria, such as *E. coli*. Therefore, the pEVP-3 vector cannot replicate in *S.*
10 *pneumoniae*. This vector also contains multiple cloning sites, and confers resistance to chloramphenicol in both a gram-negative and gram-positive bacteria, such as *S. pneumoniae*.

c) Fusion Gene Sequences

15

A fusion *ceg* gene is another example of a recombinant molecule of the invention. A fusion gene includes a *ceg* sequence operatively fused (e.g., linked) to a non-*ceg* sequence such as, for example, a tag sequence to facilitate isolation and/or purification of the expressed CEG gene product (Kroll, D.J., et al., 1993 *DNA Cell Biol* 12:441-53).

20

Alternatively, a recombinant fusion molecule has a *ceg* sequence of the invention fused to a *ceg* sequence isolated from a different microbial source. For example, the disclosed *ceg* sequences isolated from *S. pneumoniae* can be fused to a *ceg* sequence isolated from a different bacterial species.

25

3.) CEG PROTEINS AND POLYPEPTIDE MOLECULES

The invention additionally provides CEG proteins and peptide fragments thereof that are isolated or substantially purified. Embodiments of particular CEG amino acid sequences
30 are disclosed in Tables I and II (SEQ ID NOS:114-226 and SEQ ID NOS:332-436, respectively).

The present invention also includes polypeptides having sequence variations from the predicted CEG polypeptide sequences disclosed herein, including mutant variants, conservative substitution variants, and similar CEG polypeptides from other prokaryotic organisms. For convenience, such proteins are referred to herein as "CEG proteins",
5 "CEG polypeptides", or "proteins of the invention".

As used herein, CEG protein refers to a polypeptide having amino acid sequence identity or similarity to any one of the predicted amino acid sequences, as provided in SEQ ID NO.:
10 114-226 or 332-436. The variant CEG polypeptides can be allelic forms of CEG, such as mutant forms of CEG polypeptides. The present invention also provides conservative substitution-mutants of the CEG proteins that maintain functional activity of wild-type CEG (e.g., the CEG polypeptide is required for bacterial cell viability).

15 The CEG protein may be isolated from any source whether natural, synthetic, semi-synthetic, or recombinant. As used herein, "natural" refers to a polypeptide which is found in nature. Accordingly, the CEG proteins may be isolated from a prokaryotic organism, such as a bacterial strain including, but not limited to, *Streptococcus*, *Escherichia*, *Bacillus*, *Pseudomonas*, *Yersinia*, *Salmonella*, and *Streptomyces*. The CEG
20 proteins of the invention, and fragments thereof, can also be generated by recombinant methods or chemical synthesis methods.

The CEG polypeptides of the invention are essential for the viability of a bacterial cell. Further, the CEG polypeptides can exhibit at least any one of the following functions: a
25 pantothenate kinase, a Holliday Junction branch migration protein, a single stranded DNA binding protein, a phosphoglucosamine mutase, an acetyltransferase, an uridylyltransferase, a malonyl CoenzymeA:ACP transacylase, a 3-oxoacyl-ACP synthase II, a 3-oxoacyl-ACP reductase, a phosphomethylpyrimidine (HMP-P) kinase, a GTP binding protein, a ATP binding protein, or a 4-aminoimidazole carboxylase. Putative
30 functions can include, but are not limited to, sugar transferase, teichoic acid biosynthesis, ribosome recycling factor, response regulator, nicotinate phosphoribosyltransferase,

nitropropane dioxygenase, (3R)-hydroxymyristol acyl carrier protein dehydrase, sugar dehydrogenase, murein biosynthesis, cobalamin biosynthesis, ABC transporter, tRNA modification enzyme, arylsulfatase, 16S processing enzyme, tRNA methyl transferase, elongation factor P, signal recognition particle, protein export, undecaprenol kinase, SRP docking domain, diacyl glycerol kinase, dihydopicillinate reductase, HU-DNA binding protein, thiamine biosynthase, GreA transcription elongation factor, dTDP-L-rhamnose synthase, ATP-binding motif, ribose-5-p-3-epimerase-like activity, GTP pyrophosphokinase, acetyl-CoA carboxylase, O-sialoglycoprotein endopeptidase, glucosamine-fructose-6-phosphate aminotransferase, Strpn adhesion-associated ABC-permease, GTP pyrophosphokinase RelA, IMP dehydrogenase, DNA gyrase subunit B, acetyl-CoA carboxylase subunit AccD, phosphoglycerol kinase, acetyl-CoA carboxylase carbonyl transferase, phosphopanthetheine adenylyltransferase, oligopeptide transport permease subunit, translocation protein, perM permease, DNA pol III gamma and tau subunits, DNA pol III delta subunit, signal peptidase I, acetyl-coA carboxylase biotin carboxyl carrier protein, protein chain release factor-1, replicative DNA helicase, topoisomerase, pentapeptide-transferase, elongation factor G, spore coat polysaccharide biosynthesis protein C, protein release factor B, DNA polymerase III alpha subunit, phosphoprotein phosphatase, chaparonin, UDP-N-acetylmuramoylalanyl-D-glutamate-2, 6-diaminopimelate ligase, techuronic acid biosynthesis, UDP-glucose lipid carrier transferase, transcription termination factor, chromosome segregation factor, amino acid biosynthesis, HMG-CoA reductase, hypoxanthine-guanine phosphoribosyltransferase.

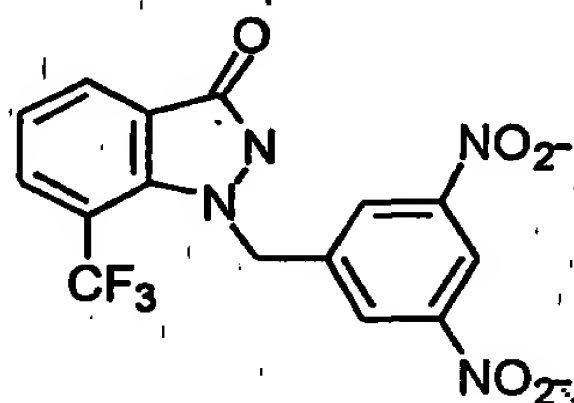
a) MODULATORS OF CEG POLYPEPTIDES

The invention provides compounds that modulate (e.g., activate or inhibit) the function of a CEG polypeptide. Such compounds can provide lead-compounds for developing drugs for diagnosing and/or treating conditions associated with bacterial infections. The modulator is a compound that may alter the function of the CEG polypeptide, such as activating or inhibiting the function of a CEG polypeptide. For example, the compound can act as agonist, antagonist, partial agonist, partial antagonist, cytotoxic agents,

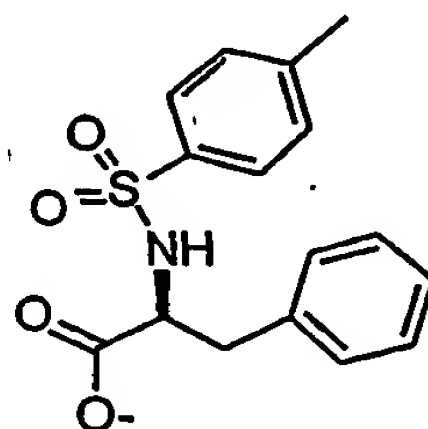
inhibitors of cell proliferation, and cell proliferation-promoting agents. The activity of the compound may be known, unknown or partially known.

Suitable ligands include, but are not limited to, diazalactones, *N*-protected amino acid,
5 azabicyclodiene, and alkaloids.

An example of a diazalactone is:

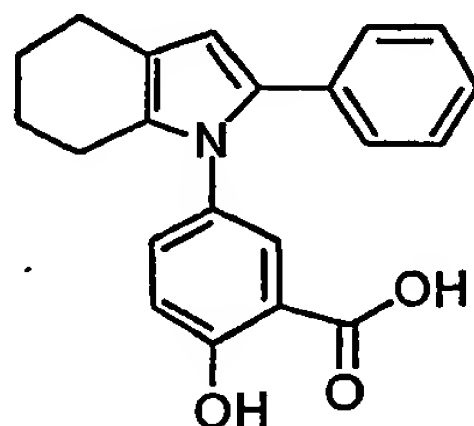


An example of a *N*-protected amino acid is:

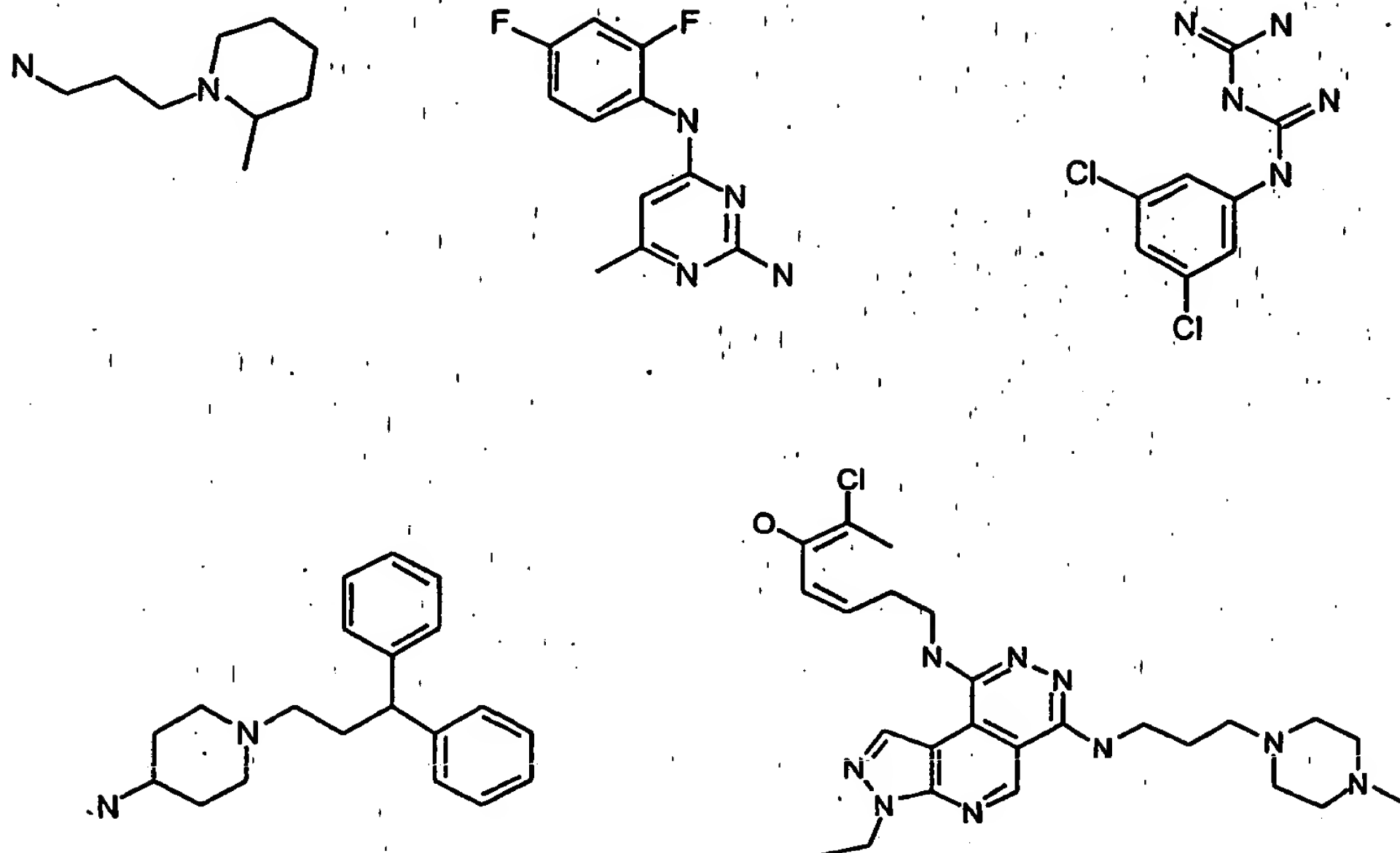


10

An example of an azabicyclodiene is:



Examples of alkaloids are:



5 B) METHODS FOR MAKING THE CEG PROTEINS AND POLYPEPTIDES

Recombinant methods are preferred if a high yield is desired. Recombinant methods involve expressing the cloned gene in a suitable host cell. For example, a host cell is introduced with an expression vector having the CEG sequence, then the host cell is cultured under conditions that permit *in vivo* production of the CEG protein. The recombinant vector can integrate the CEG sequence into the host genome. Alternatively, the CEG sequence can be maintained extra-chromosomally, as part of an autonomously replicating vector.

1. HOST-VECTOR SYSTEMS

The invention further provides a host-vector system comprising the vector, plasmid, phagemid, or cosmid comprising a *ceg* nucleotide sequence, or a fragment thereof, introduced into a suitable host cell. The host-vector system can be used to produce the

CEG polypeptides encoded by the *ceg* nucleotide sequences. The host cell can be prokaryotic or eukaryotic. Examples of suitable prokaryotic host cells include bacteria strains from genera such as *Escherichia*, *Bacillus*, *Pseudomonas*, *Streptococcus*, and *Streptomyces*. Examples of suitable eukaryotic host cells include a yeast cell, a plant cell, or an animal cell, such as a mammalian cell. A preferred embodiment provides a host-vector system comprising the pET21 vector having a *ceg* sequence introduced into an *E. coli* λ DE3 lysogen which is useful, for example for the production of the CEG protein, herein designated CFE polypeptides and CFE proteins.

- 10 Introduction of the rDNA molecules of the present invention into an appropriate cell host is accomplished by well known methods that typically depend on the type of vector used and host system employed. For example, transformation of prokaryotic host cells by electroporation and salt treatment methods are typically employed, see for example, Cohen et al., 1972 *Proc Acad Sci USA* 69:2110; Maniatis, T., et al., 1989 *Molecular Cloning, A*
- 15 *Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY. Transformation of vertebrate cells with vectors containing rDNAs, electroporation, cationic lipid or salt treatment methods are typically employed, see, for example, Graham et al., 1973 *Virol* 52:456; Wigler et al., 1979 *Proc Natl Acad Sci USA* 76:1373-76.
- 20 Successfully transformed cells, i.e., cells that contain a rDNA molecule of the present invention, can be identified by well known techniques. For example, cells resulting from the introduction of a rDNA of the present invention can be selected and cloned to produce single colonies. Cells from those colonies can be harvested, lysed and their DNA content examined for the presence of the rDNA using a method such as that described by Southern,
- 25 *J Mol Biol* (1975) 98:503, or Berent et al., *Biotech* (1985) 3:208, or the proteins produced from the cell assayed via a biochemical assay or immunological method.

Prokaryotes are generally used as host cells for cloning and producing the products of exogenous DNA sequences. For example, the *Escherichia coli* K12 BL21 (λ DE3) (Novagen) is particularly useful for expression of foreign proteins. Other strains of *E. coli*, and bacilli such as *Bacillus subtilis*, Enterobacteriaceae such as *Salmonella*

30

typhimurium or *Serratia marcescans*, various *Pseudomonas*, *Streptococcus*, and *Streptomyces* species may also be employed as host cells in cloning and expressing the recombinant proteins of this invention.

- 5 In general terms, the production of recombinant CEG proteins may involve using a host/vector system, or other methods may be used. The host/vector system may employ the following steps.

10 A nucleic acid molecule is obtained that encodes a CEG protein or a fragment thereof, such as any one of the polynucleotides disclosed in SEQ ID NOs.: 1-113 or 227-331. The CEG-encoding nucleic acid molecule is preferably inserted into an expression vector in operable linkage with suitable expression control sequences, to generate an expression vector including the CEG-encoding sequence. The expression vector is introduced into a suitable host, by standard transformation methods, and the resulting transformed host is cultured
15 under conditions that allow the production of the CEG protein. For example, if expression of the CEG gene is under the control of an inducible promoter, then suitable growth conditions would include the appropriate inducer. The CEG protein (e.g., designated a CFE polypeptide or protein), so produced, is isolated from the growth medium or directly from the cells; recovery and purification of the protein may not be necessary in some
20 instances where some impurities may be tolerated. A skilled artisan can readily adapt an appropriate host/expression system known in the art for use with CEG-encoding sequences to produce a CEG protein (Cohen, et al., *supra*; Maniatis et al., *supra*).

25 Host cells harboring the nucleic acids disclosed herein are also provided by the present invention. A preferred host is *E. coli* strain BL21(λ DE3) transfected or transformed with a vector comprising a nucleic acid of the present invention. The invention also provides a host cell capable of expressing the *ceg* sequences described herein. The preferred host cell is any strain of *E. coli* that can accommodate high level expression of an exogenously introduced gene.

30

The proteins of the present invention can also be made by chemical synthesis. The principles of solid phase chemical synthesis of polypeptides are well known in the art and may be found in general texts relating to this area (Dugas, H. and Penney, C. 1981 *Bioorganic Chemistry*, pp 54-92, Springer-Verlag, New York). CEG polypeptides may
5 be synthesized by solid-phase methodology utilizing an Applied Biosystems 430A peptide synthesizer (Applied Biosystems, Foster City, Calif.) and synthesis cycles supplied by Applied Biosystems. Protected amino acids, such as t-butoxycarbonyl-protected amino acids, and other reagents are commercially available from many chemical supply houses.

10 The polypeptides of the invention exhibit properties of a CEG protein, such as, for example, the ability to elicit the generation of antibodies that specifically bind an epitope associated with CEG polypeptides. Accordingly, the CEG polypeptide, or any oligopeptide thereof, is capable of inducing a specific immune response in appropriate
15 animals or cells and binding with specific antibodies.

C) ANTIBODIES THAT RECOGNIZE AND BIND THE PROTEINS AND POLYPEPTIDES OF THE INVENTION

20 The invention further provides antibodies (e.g., polyclonal, monoclonal, chimeric, humanized, and human antibodies) that bind a CEG polypeptide. The most preferred antibodies will selectively bind a CEG polypeptide and will not bind (or will bind weakly) a non-CEG polypeptide. Antibodies that are particularly contemplated include monoclonal and polyclonal antibodies, as well as fragments thereof (e.g., recombinant proteins) which
25 include the antigen binding domain and/or one or more complement determining regions of these antibodies. These antibodies can be from any source, for example, rabbit, sheep, rat, dog, cat, pig, horse, mouse, and human.

30 The invention encompasses antibody fragments that specifically recognize a CEG polypeptide. As used herein, an antibody fragment is defined as at least a portion of the variable region of the immunoglobulin molecule that binds to its target, i.e., the antigen binding region. Some of the constant region of the immunoglobulin may be included.

As will be understood by those skilled in the art, the regions or epitopes of a CEG polypeptide to which an antibody is directed may vary with the intended application. For example, antibodies intended for use in an immunoassay for the detection of membrane-bound CEG proteins on viable bacterial cells should be directed to an accessible epitope on membrane-bound CEG proteins. Antibodies that recognize other epitopes may be useful for the identification of CEG protein within damaged or dying cells, for the detection of secreted CEG protein or fragments thereof.

Various methods for the preparation of antibodies are well known in the art. For example, antibodies may be prepared by immunizing a suitable mammalian host using a CEG protein, peptide, or fragment, in isolated or immunoconjugated form (Harlow, 1989 *Antibodies*, Cold Spring Harbor Press, NY). In addition, fusion proteins comprising CEG polypeptides may also be used, such as a CEG protein/GST-fusion protein. Cells expressing or overexpressing a CEG polypeptide may also be used for immunizations. Similarly, any cell engineered to express CEG protein may be used. This strategy may result in the production of monoclonal antibodies with enhanced capacities for recognizing endogenous CEG protein.

The present invention contemplates chimeric antibodies that comprise a human and non-human immunoglobulin portion. The antigen combining region (variable region) of a chimeric antibody can be derived from a prokaryotic source (e.g., bacteria) and the constant region of the chimeric antibody which confers biological effector function to the immunoglobulin can be derived from a eukaryotic source (e.g., human). The chimeric antibody should have the antigen binding specificity of the prokaryotic antibody molecule and the effector function conferred by the eukaryotic antibody molecule.

In one example, the procedure used to produce chimeric antibodies can involve the following steps:

- a) Identifying and cloning the correct immunoglobulin gene segment encoding the antigen binding portion of the antibody molecule. This gene segment is known as the VDJ, variable, diversity and joining regions for heavy chains or VJ, variable,

joining regions for light chains or simply as the V or variable region. This gene regions may be in either the cDNA or genomic form;

- b) Cloning the gene segments encoding the constant region or desired part thereof;
- c) Ligating the variable region with the constant region so that the complete chimeric
5 antibody is encoded in a form that can be transcribed and translated;
- d) Ligating this construct into a vector containing a selectable marker and gene control regions such as promoters, enhancers and poly(A) addition signals;
- e) Amplifying this construct in bacteria;
- f) Introducing this DNA into eukaryotic cells (transfection) most often mammalian
10 lymphocytes;
- g) Selecting for cells expressing the selectable marker;
- h) Screening for cells expressing the desired chimeric antibody; and
- k) Testing the antibody for appropriate binding specificity and effector functions.

15 Chimeric antibodies of several distinct antigen binding specificities have been produced by protocols well known in the art, including anti-TNP antibodies (Boulianne et al., 1984 *Nature* 312:643); and anti-tumor antigen antibodies (Sahagan et al., 1986 *J. Immunol.* 137:1066). Likewise, several different effector functions have been achieved by linking new sequences to those encoding the antigen binding region. Examples of these include
20 enzymes (Neuberger et al., 1984 *Nature* 312:604); immunoglobulin constant regions from another species and constant regions of another immunoglobulin chain (Sharon et al., 1984 *Nature* 309:364; Tan et al., 1985 *J. Immunol.* 135:3565-3567). Additionally, procedures for modifying antibody molecules and for producing chimeric antibody molecules using homologous recombination to target gene modification have been
25 described (Fell et al., 1989 *Proc. Natl. Acad. Sci. USA* 86:8507-8511).

The predicted amino acid sequence of a CEG protein may be used to select specific regions of the CEG protein for generating antibodies. For example, hydrophobicity and hydrophilicity analyses of a CEG polypeptide may be used to identify hydrophobic and
30 hydrophilic regions in the CEG protein. Regions of the CEG protein that show immunogenic structure, as well as other regions and domains, can readily be identified using

various other methods known in the art, such as Chou-Fasman, Garnier-Robson, Kyte-Doolittle, Eisenberg, Karplus-Schult or Jameson-Wolf analysis. Fragments that include the immunogenic regions are particularly suited for generating specific classes of antibodies.

- 5 Methods for preparing a protein for use as an immunogen and for preparing immunogenic conjugates of a protein with a carrier such as BSA, KLH, or other carrier proteins are well known in the art. In some circumstances, direct conjugation using, for example, carbodiimide reagents may be used; in other instances linking reagents such as those supplied by Pierce Chemical Co., Rockford, IL, may be effective. Administration of a CEG
10 immunogen is conducted generally by injection over a suitable time period and with use of a suitable adjuvant, as is generally understood in the art. During the immunization schedule, titers of antibodies can be taken to determine adequacy of polyclonal antibody formation.

- While the polyclonal antisera produced in this way may be satisfactory for some
15 applications, for pharmaceutical compositions, monoclonal antibody preparations are preferred. Immortalized cell lines which secrete a desired monoclonal antibody may be prepared using the standard method of Kohler and Milstein (*Nature* 256: 495-497) or other techniques as described in *Monoclonal Antibodies; A Manual of Techniques*, CRC press, Inc., Boca Raton, Fla. (1987) ed. Zola. The immortalized cell lines secreting the desired
20 antibodies are screened by immunoassay in which the antigen is the CEG polypeptide having binding activity, or a fragment thereof. When the appropriate immortalized cell culture secreting the desired antibody is identified, the cells can be cultured either *in vitro* or by production in ascites fluid.

- 25 The desired monoclonal antibodies are then recovered from the culture supernatant or from the ascites supernatant. Fragments of the monoclonal antibodies of the invention or the polyclonal antisera (e.g., Fab, F(ab')₂, Fv fragments, fusion proteins) which contain the immunologically significant portion (i.e., a portion that recognizes and binds a CEG protein) can be used as antagonists, as well as the intact antibodies. Humanized antibodies directed
30 against a CEG polypeptide are also useful. The advantage of using humanized antibodies is that they are less immunogenic in humans. As used herein, a humanized antibody is an

immunoglobulin molecule which is capable of binding to a CEG polypeptide and which comprises a FR region having substantially the amino acid sequence of a human immunoglobulin and a CDR having substantially the amino acid sequence of non-human immunoglobulin or a sequence engineered to bind a CEG protein. Methods for humanizing murine and other non-human antibodies by substituting one or more of the non-human antibody CDRs for corresponding human antibody sequences are well known (Jones et al., 1986 *Nature* 321: 522-525; Riechman et al., 1988 *Nature* 332: 323-327; Verhoeyen et al., 1988 *Science* 239: 1534-1536; Carter et al., 1993 *Proc. Natl. Acad. Sci. USA* 89: 4285; and Sims et al., 1993 *J. Immunol.* 151:2296).

Use of immunologically reactive fragments, such as the Fab, Fab', or F(ab')₂ fragments is often preferable, especially in a therapeutic context, as these fragments are generally less immunogenic than the whole immunoglobulin. Further, bi-specific antibodies specific for two or more epitopes may be generated using methods generally known in the art. Further, antibody effector functions may be modified so as to enhance the therapeutic effect of the antibodies of the invention. For example, cysteine residues may be engineered into the Fc region, permitting the formation of interchain disulfide bonds and the generation of homodimers which may have enhanced capacities for internalization, ADCC and/or complement-mediated cell killing (Caron et al., 1992 *J. Exp. Med.* 176: 1191-1195; Shopes, 1992 *J. Immunol.* 148: 2918-2922). Homodimeric antibodies may also be generated by cross-linking techniques known in the art (Wolff et al., *Cancer Res.* 53: 2560-2565). The invention also provides pharmaceutical compositions having the monoclonal antibodies or anti-idiotypic monoclonal antibodies of the invention.

The antibodies or fragments may also be produced, using current technology, by recombinant means. Regions that bind specifically to the desired regions of the CEG protein can also be produced in the context of chimeric or CDR grafted antibodies of multiple species origin. The invention includes an antibody, e.g., a monoclonal antibody which competitively inhibits the immunospecific binding of any of the monoclonal antibodies of the invention to a CEG protein.

Alternatively, methods for producing fully human monoclonal antibodies, include phage display and transgenic methods, are known and may be used for the generation of human monoclonal antibodies (reviewed in: Vaughan et al., 1998 *Nature Biotechnology* 16: 535-539). For example, fully human monoclonal antibodies may be generated using cloning technologies employing large human Ig gene combinatorial libraries (i.e., phage display) (Griffiths and Hoogenboom, "Building an *in vitro* immune system: human antibodies from phage display libraries", in: *Protein Engineering of Antibody Molecules for Prophylactic and Therapeutic Applications in Man*, Clark, M. (Ed.), Nottingham Academic, pp 45-64 (1993); Burton and Barbas, "Human Antibodies from combinatorial libraries" *Id.*, pp 65-82). Fully human monoclonal antibodies may also be produced using transgenic mice engineered to contain human immunoglobulin gene loci as described in PCT Patent Application WO98/24893, Jakobovits et al., published December 3, 1997 (see also, Jakobovits, 1998 *Exp. Opin. Invest. Drugs* 7: 607-614). This method avoids the *in vitro* manipulation required with phage display technology and efficiently produces high affinity, authentic human antibodies.

The antibody or fragment thereof of the invention may be labeled with a detectable marker or conjugated to a second molecule, such as a therapeutic agent (e.g., a cytotoxic agent) thereby resulting in an immunoconjugate. For example, the therapeutic agent includes, but is not limited to, an anti-tumor drug, a toxin, a radioactive agent, a cytokine, a second antibody or an enzyme. Further, the invention provides an embodiment wherein the antibody of the invention is linked to an enzyme that converts a prodrug into a cytotoxic drug.

Examples of cytotoxic agents include, but are not limited to ricin, ricin A-chain, doxorubicin, daunorubicin, taxol, ethidum bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, diphtheria toxin, *Pseudomonas* exotoxin (PE) A, PE40, abrin, arbrin A chain, modeccin A chain, alpha-sarcin, gelonin, mitogellin, retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, sapaonaria officinalis inhibitor, and glucocorticoid and other chemotherapeutic agents, as well as radioisotopes such as ^{212}Bi , ^{131}I , ^{131}In , ^{90}Y , and ^{186}Re .

Suitable detectable markers for diagnostic used include, but are not limited to, a radioisotope, a fluorescent compound, a bioluminescent compound, chemiluminescent compound, a metal chelator or an enzyme. Antibodies may also be conjugated to an anti-cancer pro-drug activating enzyme capable of converting the pro-drug to its active form. See, for example, U.S. Patent Nos. 4,952,394 and 5,716,990.

Additionally, a recombinant protein of the invention comprising the antigen-binding region of any of the monoclonal antibodies of the invention can be made. In such a situation, the antigen-binding region of the recombinant protein is joined to at least a functionally active portion of a second protein having therapeutic activity. The second protein can include, but is not limited to, an enzyme, lymphokine, oncostatin or toxin. Suitable toxins include those described above.

Techniques for conjugating or joining therapeutic agents to antibodies are well known (Arnon et al., "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in: *Monoclonal Antibodies And Cancer Therapy*, Reisfeld et al. (eds.), pp. 243-56, Alan R. Liss, Inc. 1985; Hellstrom et al., "Antibodies For Drug Delivery", in: *Controlled Drug Delivery* (2nd Ed.), Robinson et al. (eds.), pp. 623-53, Marcel Dekker, Inc. 1987; Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in: *Monoclonal Antibodies '84: Biological And Clinical Applications*, Pinchera et al. (eds.), pp. 475-506 (1985); and Thorpe et al., "The Preparation And Cytotoxic Properties Of Antibody-Toxin Conjugates", in: *Immunol. Rev.*, 62:119-58 (1982)). Techniques for joining detectable markers to antibodies are also known.

D) PHARMACEUTICAL COMPOSITIONS OF THE INVENTION

The invention includes pharmaceutical compositions for use in the treatment of microbial infections comprising a pharmaceutically effective amount of an anti-CEG antibody or a CEG polypeptide.

In one embodiment, the pharmaceutical compositions may comprise a CEG antibody, either unmodified, conjugated to a therapeutic agent (e.g., drug, toxin, enzyme or second antibody) or in a recombinant form (e.g., chimeric or bispecific). The compositions may additionally include other antibodies or conjugates (e.g., an antibody cocktail).

5

The pharmaceutical compositions also preferably include suitable carriers and adjuvants which include any material which when combined with the molecule of the invention (e.g., an anti-CEG antibody or a CEG protein) retains the molecule's activity and is non-reactive with the subject's immune systems. Examples of suitable carriers and adjuvants include, but are not limited to, human serum albumin, ion exchangers, alumina, lecithin, buffer substances such as phosphates, glycine, sorbic acid, potassium sorbate, and salts or electrolytes such as protamine sulfate. Other examples include any of the standard pharmaceutical carriers such as a phosphate buffered saline solution, water, emulsions such as oil/water emulsion, and various types of wetting agents. Other carriers may also include sterile solutions, tablets including coated tablets and capsules. Typically such carriers contain excipients such as starch, milk, sugar, certain types of clay, gelatin, stearic acid or salts thereof, magnesium or calcium stearate, talc, vegetable fats or oils, gums, glycols, or other known excipients. Such carriers may also include flavor and color additives or other ingredients. Compositions comprising such carriers are formulated by well known conventional methods. Such compositions may also be formulated within various lipid compositions, such as, for example, liposomes as well as in various polymeric compositions, such as polymer microspheres.

The pharmaceutical compositions of the invention can be administered using conventional modes of administration including, but not limited to, intravenous, intraperitoneal, oral, intralymphatic or administration directly into the tumor. Intravenous administration is preferred.

The pharmaceutical compositions of the invention may be in a variety of dosage forms which include, but are not limited to, liquid solutions or suspensions, tablets, pills, powders, suppositories, polymeric microcapsules or microvesicles, liposomes, and

injectable or infusible solutions. The preferred form depends upon the mode of administration and the therapeutic application.

The CEG polypeptides and proteins of this invention are found in common pathogenic bacterial species such as *Streptococcus pneumoniae*. This organism causes upper respiratory tract infections. Thus, the peptides and proteins of this invention can be used as immunogens in subunit vaccines for vaccination against a pathogenic bacteria such as *Streptococcus pneumoniae*. Additionally, the *ceg* sequences of the invention can be used as DNA vaccines (U.S. Patent No. 5,736,524 and U.S. Patent No. 5,989,553).

The polypeptides and proteins of this invention can be formulated as univalent and multivalent vaccines. The protein can be mixed, conjugated or fused with other antigens, including B or T cell epitopes of other antigens.

Further, when a haptenic peptide of the proteins of the invention is used, (i.e., a peptide which reacts with cognate antibodies, but cannot itself elicit an immune response), it can be conjugated to an immunogenic carrier molecule. Conjugation to an immunogenic carrier can render the oligopeptide immunogenic. Examples of carrier molecules are tetanus toxin or toxoid, diphtheria toxin or toxoid and any mutant forms of these proteins such as CRM.sub.197. Others include exotoxin A of *Pseudomonas*, the heat labile toxin of *E. coli* and rotaviral particles (including rotavirus and VP6 particles). Alternatively, a fragment or epitope of the carrier protein or other immunogenic protein can be used. For example, the happen can be coupled to a T cell epitope of a bacterial toxin.

In formulating the vaccine compositions with the CEG polypeptides or proteins of the invention, alone or in the various combinations described, the immunogen is adjusted to an appropriate concentration and formulated with any suitable vaccine adjuvant. Suitable adjuvants include, but are not limited to: surface active substances, e.g., hexadecylamine, octadecylamine, octadecyl amino acid esters, lysolecithin, dimethyl-di-octadecylammonium bromide), methoxyhexadecylglycerol, and pluronic polyols; polyamines, e.g., pyran, dextransulfate, poly. IC, carbopol; peptides, e.g., muramyl

dipeptide, dimethylglycine, tuftsin; oil emulsions; and mineral gels, e.g., aluminum hydroxide, aluminum phosphate, etc. and immune stimulating complexes. The immunogen may also be incorporated into liposomes, or conjugated to polysaccharides and/or other polymers.

5

The vaccines can be administered to a human or animal in a variety of ways. These include intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, oral and intranasal routes of administration. Further, the vaccines can be live or inactivated vaccines.

10

The most effective mode of administration and dosage regimen for the compositions of this invention depends upon the severity and course of the disease, the patient's health and response to treatment and the judgment of the treating physician. Accordingly, the dosages of the compositions should be titrated to the individual patient.

15

E) USES OF THE MOLECULES OF THE INVENTION

1) MOLECULAR WEIGHT MARKERS

20 The nucleic acid molecules of the invention and their encoded proteins may be employed as molecular weight markers. For example, the molecular weight of each of the nucleic acid molecules having *ceg* sequences and their predicted polypeptides can be determined and can be used to compare against other gene sequences and proteins whose molecular weights are unknown.

25

2) DIAGNOSTICS

The nucleic acid molecules of the invention may be employed in diagnostic embodiments. For example, the presence of nucleotide sequences which are identical or
30 similar to the *ceg* sequences of the invention may be detected within a biological sample.

The biological sample may include blood, serum or a swab from nose, ear or throat, may be determined by means of a nucleic acid detection assay.

5 Nucleic acid probes or primers having sequences complementary to *ceg* sequences may be used in a hybridization assay to detect the presence of the sequences which are identical or similar to the *ceg* sequences of the invention in the biological samples. Typically, nucleic acids molecules obtained from a suitable biological sample are hybridized with labeled probes or primers. The resulting hybridized molecules are detected and resolved by methods well known in the art, such as Northern or Southern
10 blotting, micro-array technology, or amplifying with PCR technology. Other hybridization techniques and systems are known that can be used in connection with the detection aspects of the invention, including diagnostic assays such as those described in Falkow et al., U.S. Pat. No. 4,358,535.

15 Examples of the PCR technology are disclosed in U.S. Patent Nos. 4,683,202 and 4,965,188 (incorporated herein by reference). Generally, nucleic acid molecules are obtained from a suitable biological source and contacted with two primers corresponding to the *ceg* sequences disclosed herein, under conditions which allow for hybridization and polymerization to occur. A pair of probes, one corresponding to the 5' flanking region
20 and the other corresponding to the 3' flanking region, would be sufficient to detect the nucleic acid molecules of the invention in a biological sample and may be used to indicate the amount of bacteria present.

Alternative methods of detecting nucleic acid molecules include, for example, in situ
25 hybridization techniques, where a *ceg* probe is used to detect homologous sequences within one or more cells, such as cells within a clinical sample or even cells grown in tissue culture. As is well known in the art, the cells are prepared for hybridization by fixation, e.g. chemical fixation, and placed in conditions that allow for the hybridization of a detectable probe with nucleic acids located within the fixed cell.

30

The amount of *ceg* sequences present in a biological sample can be quantified and compared to the levels in a normal or "healthy" sample. For example, *ceg* sequences present in either increased or decreased levels, compared to the levels found in the control sample may indicate the presence of bacteria. This information is useful for diagnosis of a bacterial infection that requires treatment with an antibacterial agent.

Alternatively, the amount of CEG polypeptides present in a biological sample may be determined by means of an immunoassay. For example, labeled antibodies reactive against CEG polypeptides may be used in an immuno-reactive assay to detect the presence of CEG polypeptides in the biological samples.

3) SCREENING CANDIDATE CEG SEQUENCES

a) Gene Disruption Assay

The *ceg* nucleotide sequences of the invention can be used to identify nucleotide sequences which are identical or similar to the *ceg* sequences that are required for bacterial cell viability. For example, the *ceg* sequences can be used in a bacterial gene disruption assay to screen candidate nucleotide sequences to identify sequences required for bacterial cell viability.

The disruption assay can involve: introducing into a host cell a recombinant vector that is capable of integration into the host genome, where the recombinant vector includes a candidate sequence that putatively encodes a cell-viability gene product (e.g., the exogenous *ceg* sequence); the vector integrates the candidate sequence into a target sequence within the host's genome (e.g., the endogenous *ceg* sequence); and the host cell, so introduced, is screened for viability. The recombinant vector preferably includes a selectable marker so that the introduced host cell can be screened for viability in the presence of a selectable agent.

For example, Figure 1 shows a schematic representation of a gene disruption assay, within a bacterial host cell. In Figure 1A, the recombinant vector, pEVP3, includes the CAT gene (e.g., the selectable marker chloramphenicol acetyl transferase) and an internal region of the *ceg* disrupting sequence; the internal region excludes the 5' and 3' ends of the *ceg* sequence. The "X" in Figure 1 indicates the recombinant pEVP3 vector undergoing homologous recombination with the target sequence (e.g., within the host genome). In Figure 1B, the resolved pEVP3 vector that is integrated into the host genome, is shown. Left to right are the following elements: the native promoter of the target gene; a 5' partial copy of the target gene; the body of the integrated pEVP3 vector including the disrupting gene and CAT; and, a 3' partial copy of the target gene. Thus, integration of the pEVP3 vector via homologous recombination results in two partial gene duplications flanking the integrated vector. If the target gene is not essential for survival, it is possible to recover chloramphenicol-resistant colonies of *S. pneumoniae*. Failure to recover chloramphenicol resistant colonies, in the presence of the proper controls as described below, indicates that the target gene may be essential for cell viability.

More particularly, the gene disruption assay for screening candidate *ceg* sequences can involve the following steps. The recombinant pEVP-3 vector encoding CAT resistance and having a fragment of a candidate *ceg* sequence, can be introduced into transformation-competent *S. pneumoniae* cells by methods that are well-known in the art (Lee, M.S., et al., 1998 *Appl. Environ. Microbiol.* 64:4796-4802). The preferred size of the *ceg* fragment can be between about 200 to about 500 bp in length. It is advantageous that the candidate *ceg* sequence does not include the 5' and 3' ends that encode the N- and C-terminal ends of the CEG polypeptide. This insures that the inserted *ceg* fragment and the disrupted endogenous *ceg* gene sequence are not capable of expression of a full-length, functional *ceg* gene product. The transformation-competent cells can be obtained by performing the transformation step in the presence of a heptadecapeptide that induces competence for transformation of *S. pneumoniae* (Havarstein, L. S., et al., 1995 *Proc. Nat'l. Acad. Sci.* 92:11140-11144), such as the CSP-1 peptide. The CSP-1 can be naturally-derived or synthetic. Additionally, the transformation step can be optimized by performing the transformation when the cells have reached a density which is optimal for

transformation (e.g., 3×10^7 cells per ml.) (Havarstein, L. S. et al. *supra*). The recombinant vector can be introduced into the competent pneumococci and may undergo homologous recombination, whereby the candidate *ceg* fragment recombines with the corresponding endogenous *ceg* sequence, resulting in targeted integration of the vector
5 into the pneumococcal genome and disruption of the endogenous *ceg*.

The transformed cells can be plated on or cultured in chloramphenicol-containing growth medium. The cells can be cultured under standard conditions, such as 37° C in 5% CO₂ for approximately 40 to 48 hours, for the purpose of selecting cells that carry the
10 integrated vector.

Additionally, control samples can be run in parallel with the gene disruption assay, in order to determine whether the gene disruption procedure is working properly. For example, the control samples can be used to calibrate the gene disruption experiment so
15 that disruption of a known non-essential bacterial gene results in an approximate number of colonies per plate. Similarly, the disruption of a known essential gene can be calibrated to yield only zero or one colony per plate. The appearance of one colony is due to the rare illegitimate recombination into a non-homologous sequence. In particular, a known non-essential gene such as the *lytA* gene (Tomasz, A., et al., 1988 *J. Bacteriol.*
20 170:5931-5934) can be used so that between about 70 to 100 chloramphenicol-resistant colonies will grow per plate. Similarly, the *ftsZ* gene (Lutkenhaus, J. F., et al., 1980 *J. Bacteriol.* 143:1281-1288), a known essential gene, can be used to yield zero or, rarely, one colony per plate. As is well known in the art, specific parameters that are involved in any given gene disruption assay can be adjusted to calibrate the desired number of plated
25 cells in the control samples. Experimental parameters that can be adjusted include, but are not limited to, the *E. coli* strain used to propagate the vector/insert, the fragment length of the sequence to be integrated, the amount of recombinant integration vector used to transform the cells, use of transformation-competent cells, and plating density of the transformed cells.

30

The transformed cells carrying the recombinant integration vector that disrupts expression of an endogenous essential gene (e.g., the target *ceg* gene) can be identified, based on a selectable phenotype such as non-viability. For example, the cells that carry a disrupted non-essential gene will be viable and, due to the integration of pEVP3, will grow on chloramphenicol-containing medium. In contrast, cells that carry a disrupted essential gene will not grow (e.g., non-viable) on the chloramphenicol-containing medium. Thus, the transformed cells that do not grow under these selective conditions carry an endogenous gene sequence that is essential for cell viability which has been disrupted by an exogenous candidate fragment, thereby identifying a *ceg* sequence. Steps one through three may be repeated in order to confirm that the *ceg* sequences, so identified, are essential for cell viability.

b) Autolysin Assay

It is advantageous to perform additional steps to determine whether the homologous recombination events result in disruption of the intended target gene sequence. The *lytA* transformation control can be used to confirm that the transformation system is functioning properly. For example, a phenotypic test for autolysin activity (*lytA* gene product) can be performed to determine that the exogenous *lytA* fragment is correctly integrated into the *lytA* site within the host genome. This typically involves flooding the culture plates containing transformants carrying the integrated *lytA* control vector with a solution of detergent, such as 0.1% deoxycholate, which triggers cell lysis in *lytA*-intact cells (e.g., the cells that have not undergone homologous recombination). After about 5-10 minutes the colonies with intact *lytA* will appear ghost-like due to cell lysis, and the colonies with a disrupted *lytA* gene will appear intact.

c) Polarity Analysis

The *ceg* sequences that are confirmed to be essential for cell viability can be examined further by performing a polarity analysis to determine if the corresponding endogenous *ceg* sequence is organized in an operon. Polarity is an effect unique to prokaryotes and is

the result of the operon organization of bacterial genomes. Many bacterial genes are arranged in operons in which multiple genes are under the control of a single regulatory sequence (e.g., a promoter) and are transcribed into a single mRNA transcript. With respect to the orientation of multiple genes within an operon, the genes that are proximal to the regulatory sequence are said to be "upstream" genes and the genes that are distal are said to be "downstream" genes. For example, many operons contain genes encoding different proteins that catalyze discrete steps of a common biochemical pathway. Thus, any of the proteins that catalyze the steps of the pathway may be essential for cell viability.

The presence of operons in a bacterial host genome may influence the interpretations of the gene disruption results. For example, disruption of an upstream gene may be erroneously interpreted as affecting the expression of the disrupted gene but may, in fact, have expression affects on the intact downstream genes. Therefore, it is advantageous to perform a polarity analysis to determine if a *ceg* sequence is part of an operon.

A polarity analysis can involve performing an *in vivo* gene disruption procedure using, as the disrupting sequence, a *ceg* sequence that includes the entire *ceg* coding sequence region but lacking expression regulatory sequences. This differs from the gene disruption assay, which involves the central region of the *ceg* sequence. The polarity analysis involves gene duplication via homologous recombination. For example, the pEVP-3 vector having the entire coding region of a *ceg* sequence can be used for the polarity analysis (Figure 2 A). The polarity analysis will yield different results depending on the organization of the endogenous target sequence within the host genome.

For example, Figure 2 shows a schematic representation of the polarity test for operons, within a bacterial host cell. In Figure 2A, the recombinant vector, pEVP3, includes the CAT gene and the entire coding region of the *ceg* disrupting sequence. The "X" in Figure 2 indicates the recombinant pEVP3 vector undergoing homologous recombination with the target sequence. Two of the possible results of homologous recombination are shown in Figures 2 B and C.

In Figure 2 B, case 1, if the endogenous target sequence is not organized in an operon, the integration event may yield: a functional target sequence (e.g., it is capable of expression); a duplicate non-functional target sequence that lacks a promoter; and a functional downstream gene (e.g., Gene B) that is controlled by its own promoter. The cells carrying this type of integrated target sequence can be recovered as viable cells that grow in the presence of chloramphenicol; this condition is termed "polarity negative".

In Figure 2 C, case 2, if the target sequence is organized in an operon, then the integration event may yield an integration site that is similar to that described for case 1, including: a functional target sequence; and a duplicate non-functional target sequence which is not functional. However, this integration event may also yield a non-functional downstream gene (e.g., Gene B) because expression of this downstream gene is controlled by a promoter located upstream of the insertion site. The cells that carry this type of integrated target sequence will be non-viable; this condition is termed "polarity positive". Thus, the polarity analysis provides a method to determine whether integration of a recombinant vector into a target *ceg* sequence effects expression of downstream genes.

The *ceg* sequences disclosed herein (SEQ ID NOs.: 1-113, 227-331) encode gene products that are essential for viability in *S. pneumoniae*. Furthermore, many of these *ceg* sequences have been analyzed for the polarity effect and the results are presented in Table I. One subset of *ceg* sequences is classified as polarity negative (-), since the homologous recombination event did not effect the expression of downstream genes. Another subset of *ceg* sequences is classified as polarity positive (+), since the homologous recombination event did affect the expression of downstream genes. The *ceg* sequences that have not yet been classified as polarity positive or negative are indicated in Table I as a blank. For the *ceg* sequences that are classified as polarity positive, the genes downstream of the disrupted endogenous *ceg* sequences may or may not also be essential.

4) ASSAYS FOR IDENTIFYING CEG LIGANDS AND OTHER BINDING AGENTS

- The present invention provides screening methods for identifying agents that interact and/or bind to the CEG proteins of the invention, such as a ligand. An agent can be, for example, a natural product, a derived or synthetic chemical molecule, a polypeptide, a nucleic acid molecule, or a metal. The agents that interact with CEG proteins may cause bacterial cell death by disrupting the functions of CEG proteins, including, but not limited to, nucleotide biosynthesis, DNA replication, RNA transcription, protein translation, and/or cell wall biosynthesis. Accordingly, the present invention provides screening methods for identifying agents having antibacterial activity, such as agents that cause bacterial cell death by interacting with the CEG proteins. These antibacterial agents are useful for treating diseases and afflictions associated with bacterial infections.
- Various methods can be used to discover agents having antibacterial activity, as determined by the ability of the binding agent to bind to a CEG protein and disrupt the function of the CEG protein. These screening methods include whole cell *in vivo* assays as well as *in vitro* assays with cellular components.
- An *in vivo* screening method for identifying ligands that bind CEG polypeptides can be performed in a whole cell assay. A typical method may be the use of whole bacterial cells to assess the antibacterial properties based on cell growth or viability. These methods can include methods for measuring cell growth and/or viability, for example, by optical density or zones of growth (Koch, A. L. et al., 1970 *Anal. Biochem.* 38:252-259; Biemer, J. J. et al., 1973 *Ann. Clin. Lab. Sci.* 2:135-140; *Manual of Clinical Microbiology*; 7th edition, Murray, P. R. (ed), ASM Press), by growth inhibition in an agar assay (Murray, P. R., *supra*), or other means of detecting cell metabolism (Mychajlonka, M. et al., 1980 *Antimicrob. Agents Chemother.* 17:572-582), and are well known to those skilled in the art. In addition, there are molecular biology-based detection methods for use with whole bacterial cells, such as gene reporter assays, to monitor the effect of the ligand on specific targets (Slauch, J. M., et al., 1991 *Methods Enzymol.* 204:213-248). Examples of the reporter genes include, but are not limited to, beta-

galactosidase, alkaline phosphatase, luciferase, and green fluorescent protein. For example, one embodiment provides a reporter system that monitors inhibition of DNA synthesis by fusing a reporter such as beta-galactosidase (*lacZ*) to genes known to be upregulated by the cessation of DNA synthesis as a result of the binding of ligands to the DNA synthetic apparatus. (Shurvinton, C. E., et al., 1982 *Mol. Gen. Genetics* 185:352-355; Rosato, A., et al., 1998 *Antimicrob. Agents Chemother.* 42:1392-1396).

Alternatively, the yeast two-hybrid system (Fields, S. and Song, O. 1989, *Nature* 340:245-246) may be adapted to screen for ligands that bind CEG polypeptides. Generally, the yeast two-hybrid system is performed in a yeast host cell carrying a reporter gene, and is based on the modular nature of the GAL transcription factor which has a DNA binding domain and a transcriptional activation domain. The yeast two-hybrid system relies on the physical interaction between a recombinant polypeptide that comprises the GAL DNA binding domain and another recombinant polypeptide that comprises the GAL transcriptional activation domain. The physical interaction between the two recombinant polypeptides reconstitutes the transcriptional activity of the transcription factor, thereby causing expression of the reporter gene. Either of the recombinant polypeptides used in the two-hybrid system can be generated to include a CEG polypeptide sequence to screen for binding partners of CEG.

Another method uses the bacterial CEG proteins as the basis for *in vitro* assay systems to detect binding agents. Typically, the *in vitro* screening method comprises: a) generating the CEG protein of the invention, or membranes enriched in the CEG protein; b) exposing the CEG protein or membranes to a candidate agent; and c) detecting the interaction of the CEG protein with the agent by any suitable means. Additionally, the screening methods may be adapted to automated high-throughput procedures, such as PANDEX.RTM Baxter-Dade Diagnostics, allowing for efficient high-volume screening of candidate agents.

An alternative method for screening potential ligands involves an *in vitro* binding procedure. Typically, the CEG proteins of the invention can be produced using

recombinant DNA technology and host-vector systems as described herein. A candidate agent is introduced into a reaction vessel containing the CEG protein, or fragment thereof; the candidate agents may be detectable by methods such as, but not limited to, radioisotope or chemical labeling. Binding of the CEG protein by a candidate agent can
5 be determined by any suitable means, including, for example, quantifying bound label versus unbound label using any suitable method. Binding of a candidate agent may also be detected by methods similar to an alternative physical method disclosed in U.S. Patent No. 5,585,277. In this method, binding of a candidate agent to a protein is assessed by monitoring the ratio of folded protein to unfolded protein, for example by monitoring
10 sensitivity of the protein to a protease, or amenability to binding of the protein by a specific antibody against the folded state of the protein, or binding to chaperone protein, or by binding to any suitable surface.

The invention provides methods of identifying compounds that modulate (e.g., activate or
15 inhibit) the function of a CEG polypeptide. Essentially any compound can be used in the assays of the invention. The preferred compounds are those that are soluble in aqueous or organic solutions. It will be appreciated by those of skill in the art that there are many commercial suppliers of chemical compounds that can be used in the methods of the invention, including Sigma Chemical Co. (St. Louis, Mo.), Aldrich Chemical Co. (St.
20 Louis, Mo.), Sigma-Aldrich (St. Louis, Mo.), Fluka Chemika-Biochemica Analytika (Buchs, Switzerland), and the like.

The present invention provides methods for detecting compounds which are identified as modulators of CEG function. The methods of the invention can be performed using
25 isolated CEG polypeptides, or use whole cells expressing the CEG polypeptide. The steps of the method using isolated CEG polypeptides include: contacting the isolated CEG polypeptide with a candidate compound; and determining whether the function of the CEG polypeptide is altered. The steps of the method using whole cells include: contacting the whole cells with a candidate compound; and determining whether the cell
30 dies, indicating the compound inhibited the function of a CEG polypeptide.

The preferred methods of the invention provide high-throughput screening assays for identifying compounds which modulate the function of a CEG polypeptide. The high throughput methods permit screening of large libraries of compounds. For example the high throughput methods can use automated assay steps. The assays can be performed in parallel on a solid support, as microtiter formats on microtiter plates in robotic assays are well known. A preferred embodiment of the methods includes adapting the methods to use microtiter plates or pico- nano- or micro-liter arrays. In high throughput assays it is desirable to run positive controls to ensure that the components of the assays are working properly.

The high throughput screening methods of the invention include providing a combinatorial library containing a large number of compounds (candidate modulator compounds) (Borman, S, C. & *E. News*, 1999, 70(10), 33-48). Such combinatorial chemical libraries can be screened in one or more assays to identify library members (particular chemical species or subclasses) that exhibit the ability to modulate the function of the CEG polypeptide (Borman, S., *supra*; Dagani, R. C. & *E. News*, 1999, 70(10), 51-60). The compounds, so identified, can serve as lead-compounds or can themselves be used as potential or actual therapeutics.

A combinatorial chemical library is a collection of diverse chemical compounds generated by using either chemical synthesis or biological synthesis, to combine a number of chemical building blocks, such as reagents. For example, a linear combinatorial chemical library, such as a polypeptide library, is formed by combining a set of chemical building blocks (amino acids) in every possible way for a given compound length (i.e., the number of amino acids in a polypeptide compound). Millions of chemical compounds can be synthesized through such combinatorial mixing of chemical building blocks.

Preparation and screening of combinatorial chemical libraries is well known to those of skill in the art. Such combinatorial chemical libraries include, but are not limited to, peptide libraries (see, e.g., U.S. Pat. No. 5,010,175, Furka, *Int. J. Pept. Prot. Res.*, 1991, 37:487-493 and

Houghton, et al., *Nature*, 1991, 354, 84-88). Other chemistries for generating chemical diversity libraries can also be used. Such chemistries include, but are not limited to, peptoids (PCT Publication No. WO 91/19735); encoded peptides (PCT Publication WO 93/20242); random bio-oligomers (PCT Publication No. WO 92/00091); benzodiazepines (U.S. Pat. No. 5,288,514); diversomers, such as hydantoins, benzodiazepines and dipeptides (Hobbs, et al., *Proc. Nat. Acad. Sci. USA*, 1993, 90, 6909-6913); vinylogous polypeptides (Hagihara, et al., *J. Amer. Chem. Soc.* 1992, 114, 6568); nonpeptidal peptidomimetics with *beta*-D-glucose scaffolding (Hirschmann, et al., *J. Amer. Chem. Soc.*, 1992, 114, 9217-9218); analogous organic syntheses of small compound libraries (Chen, et al., *J. Amer. Chem. Soc.*, 1994, 116, 2661; Armstrong, et al. *Acc. Chem. Res.*, 1996, 29, 123-131); or small organic molecule libraries (see, e.g., benzodiazepines, Baum *C&E News*, 1993, Jan. 18, page 33,); oligocarbamates (Cho, et al., *Science*, 1993, 261, 1303); and/or peptidyl phosphonates (Campbell, et al., *J. Org. Chem.* 1994, 59, 658); nucleic acid libraries (see, Seliger, H et al., *Nucleosides & Nucleotides*, 1997, 16, 703-710); peptide nucleic acid libraries (see, e.g., U.S. Pat. No. 5,539,083); antibody libraries (see, e.g., Vaughn, et al., *Nature Biotechnology*, 1996, 14(3), 309-314 and PCT/US96/10287); carbohydrate libraries (see, e.g., Liang, et al., *Science*, 1996, 274, 1520-1522 and U.S. Pat. No. 5,593,853, Nilsson, UJ, et al., *Combinatorial Chemistry & High Throughput Screening*, 1999 2, 335-352; Schweizer, F; Hindsgaul, O. *Current Opinion In Chemical Biology*, 1999 3, 291-298); isoprenoids (U.S. Pat. No. 5,569,588); thiazolidinones and metathiazanones (U.S. Pat. No. 5,549,974); pyrrolidines (U.S. Pat. Nos. 5,525,735 and 5,519,134); morpholino compounds (U.S. Pat. No. 5,506,337); benzodiazepines (U.S. Pat. No. 5,288,514); and other similar art.

Devices for the preparation of combinatorial libraries are commercially available (see, e.g., 357 MPS, 390 MPS, Advanced Chem. Tech, Louisville Ky., Symphony, Rainin, Woburn, Mass., 433A Applied Biosystems, Foster City, Calif., 9050 Plus, Millipore, Bedford, Mass.). In addition, numerous combinatorial libraries are themselves commercially available (see, e.g., ComGenex, Princeton, N.J., Asinex, Moscow, Ru, Tripos, Inc., St. Louis, Mo., ChemStar, Ltd., Moscow, RU, 3D Pharmaceuticals, Exton, Pa., Martek Bio sciences, Columbia, Md., etc.).

In the high throughput methods of the invention, several thousand different candidate compounds can be screened in a relatively short period of time. For example, each well of a microtiter plate can be used to run a separate assay against a selected potential modulator, or if concentration or incubation time effects are to be observed, every 5-10 wells can test a single modulator. Thus, a single standard microtiter plate can assay about 100 (96) modulators. If 1536 well plates are used, then a single plate can easily assay from about 100 to about 1500 different compounds. It is possible to assay many different plates per day; assay screens for up to about 6,000-20,000, and even up to about 100,000-1,000,000 different candidate modulator compounds are possible using the methods of the invention.

The following examples are presented to illustrate the present invention and to assist one of ordinary skill in making and using the same. The examples are not intended in any way to otherwise limit the scope of the invention.

EXAMPLE 1

The following provides a general description of how a list of candidate *ceg* sequences was generated. The list was generated by selecting candidate *ceg* gene sequences from a Concordance web engine using the method described in: Brucoleri, R.E., Dougherty, T.J., Davison, D.B. (1998) "Concordance analysis of microbial genomes" in: *Nucleic Acids Res* 26:4482-4486.

Microbial Genomics CEG Discovery Process Summary.

Microbial Concordance Analysis

The entire genomic sequence data of various bacteria was acquired from several public and proprietary sequence database sources, including GTC (Genome Therapeutics Corporation), and TIGR (The Institute for Genomic Research).

Predicted ORFs from the genomic data were identified, translated, and stored. The desirable ORFs were at least 90 amino acid residues in length. Concordance analysis was performed among bacteria and various parameters were used to filter out genes with high similarity to eukaryotes.

5

Concordance Analysis

The entire genomic sequence of various Eubacteria was acquired from several public and private sources. The proprietary PathoGenome System from Genome Therapeutics Corporation, Waltham, MA, USA contributed data. Public data was obtained from GenBank (<http://ncbi.nlm.nih.gov>), The Institute for Genomic Research (TIGR), the Yeast Proteome Database, from Proteome, Inc. of Beverly, MA, and the Sanger Center of the Medical Research Council of the United Kingdom (<http://www.sanger.ac.uk>). Additionally, the non-microbial sequence data used as a basis for comparison and data subtraction was obtained from a proprietary database, including the LifeSeq Database from Incyte Pharmaceuticals, Palo Alto, CA.

Where required, Incyte nucleotide sequences were translated into protein sequences in all six possible reading frames. GTC supplied predicted protein sequences with their data. In the case of other eubacterial nucleotide sequences, the program CRITICA (Badger, J. and Olsen, G., 1999 "CRITICA: coding region identification tool invoking comparative analysis" in: *Molecular Biology and Evolution* 16:512-524). The sequences were stored in flat files on a Unix computer system. Each predicted amino acid sequence had to be greater than 90 amino acids.

25

Each predicted protein sequence was compared to every other sequence (an "all-against-all" comparison). The program used was FASTA (Pearson, W.R., "Flexible sequence similarity searching with the FASTA3 program package." *Methods in Molecular Biology* 2000 132:185-219.) The parameters used were ktup=2, and all scores above the default cutoff were kept. The output was processed and stored in a PostGres 95 database (<http://www.postgresql.org>). Graphical user interfaces, using web browser technology, were constructed to query the database.

A Concordance Analysis was performed on the data. The question used to generate the dataset was show all *Streptococcus pneumoniae* open reading frames with a similarity
5 greater than or equal to 30% overall protein sequence identity to both selected gram-positive and/or gram-negative bacteria in the database. The data was further required not to match yeast or human sequences at greater than 30% overall protein sequence similarity. The resulting dataset included a list of more than 400 conserved amino acid sequences having known or unknown function. The amino acid sequences having
10 unknown functions formed the basis of a list designated Conserved Unknown Reading Frames, or CURFs which is a subset of the total list of CEGs (e.g., CURFs includes known and unknown).

The resulting list of conserved genes (e.g., more than 400 sequences) was used as a basis
15 for selecting and screening bacterial gene sequences that are essential for cell viability. The Concordance system was designed to permit high-throughput identification of conserved gene sequences in the database. (Brucoleri, R, Dougherty, T, and Davison, D. 1998 "Concordance analysis of microbial genomes" *Nucleic Acids Res.* 26:4482-4486.)

20 Data Curation And Analysis

Exact N-terminal and C-terminal translational start sites of genes were identified by pairwise similarity searches, multiple sequence alignments. Ribosome binding sites, terminators, nearby genes, operons were identified.

25

The resulting list of conserved genes was used as a basis for selecting and screening bacterial gene sequences that are essential for cell viability. This Concordance system was designed to permit high throughput use of the conserved gene sequences contained on the list. A set of Knockout PCR primers were generated, based on the list of
30 conserved genes, for the purpose of use in the gene disruption procedure described below. The PCR primers were designed to amplify a central 300-500 bp region of the *ceg* (to prevent generation of a functional copy of the *ceg* gene following integration),

ordered electronically, the primers were placed in a 96-well format, and used in the gene disruption procedure as described below.

EXAMPLE 2

The following provides a description of the procedure to generate recombinant vectors of pEVP-3 having inserts of candidate *ceg* nucleotide sequences. The Knockout primers generated by the method described in Example 1 above were used to generate DNA fragments comprising candidate *ceg* sequences.

Genomic PCR Knockout Target Fragment Generation

96-well plate format were set up (36 μ l H₂O, 5 μ l 10 \times VentTM buffer, 1 μ l gene specific, knockout forward primer (0.5 μ g/ μ l), 1 μ l gene specific knockout reverse primer (0.5 μ g/ μ l), 0.5 μ l VentTM DNA polymerase (2000 U/ml New England Biolabs, Beverly, MA), 1.5 μ l each dNTPs (10mM; 6.0 μ l total), 0.5 μ l *S. pneumoniae* chromosomal DNA (0.5 μ g/ μ l), 50 μ l total volume/reaction).

The nucleotide sequences of the forward and reverse knockout primer pairs were generated from the nucleotide sequence information obtained from the Genomic Therapeutics Corporation database for *Streptococcus pneumoniae*. The primer pairs were each used in a PCR reaction to generate a unique internal (e.g., central region) fragment of the candidate gene targeted for knockout.

The PCR program was set in the PCR machine (Initial 95 °C - 5 minutes; 30 Cycles of: 95 °C - 1 minute, 58 °C - 1 minute, 72 °C - 30 seconds; Final, 72 °C - 10 minutes, 4 °C - hold indefinitely). 5 μ l of each reaction was run on an 0.8% agarose gel after purifying fragment over PCR purification kit (Qiagen) to visualize the fragments then ligation reactions were performed.

Ligation Reactions proceeded (set up in 96-well plate format (10.0 μ l genomic PCR fragment (generated from step 2 above), 1.0 μ l pEPV-3 SmaI-cut vector (1:10 dilution of vector DNA at 50-100 ng/ μ l), 1.5 μ l 10 \times ligation buffer (New England Biolabs™), 1.0 μ l T4 DNA Ligase (New England Biolabs™ 400,000 U/ml), 1.5 μ l ddH₂O, 15.0 μ l total reaction volume).

Reactions were allowed to incubate in 96-well plate at 14 °C overnight in the PCR machine. Transformations into *E. coli* for in vivo amplification were proceeded the following day.

The nucleotide sequences of the forward and reverse primer pairs used for the polarity test were generated in a similar manner, from the nucleotide sequence information obtained from the Genomic Therapeutics Corporation database for *Streptococcus pneumoniae*. The primer pairs were each used in a PCR reaction to generate a unique fragment of the candidate gene targeted for the polarity test. The fragment generated for the polarity test included the entire *ceg* coding sequence region but lacking the expression regulatory sequences.

Transformation into *E. coli* (strain LE392):

The next day, 3 μ l of above ligation mix was used per transformation reaction plus 50 μ l LE392 competent cells. Reactions were set up in 96-well plate format; incubated on ice for 30 minutes; heat-shocked at 42° C for 90 seconds; and incubated on ice 2 minutes; 100 μ l SOC media (Gibco BRL) was added; then incubated at 37° C on platform shaker for 1 hour; plated on LB/chloramphenicol (13.0 μ g/ml) agar plates for constructs overnight at 37° C with plates inverted and proceeded with colony PCR to confirm constructs. The universal primers flanking the insert site in pEVP-3 were used for PCR amplification.

The colony PCR involved the following. 96-well plate format was set up (36.5 μ l H₂O, 0.5 μ l pEPV3 forward primer (0.25 μ g/ μ l), 0.5 μ l pEPV3 reverse primer (0.25 μ g/ μ l), 1.5

µl each (6.0 µl total) dNTPs (10 mM), 0.5 µl Vent™ DNA polymerase, 5 µl 10× Vent™ buffer, 1 µl of a 1:50 cell dilution, 50 µl total volume).

pEPV3 forward primer: 5' CATCAAGCTTATCGATACCGTCG 3' (SEQ ID NO:437)

5 p EPV3 reverse primer: 5' CACAGTAGTTCACCACCTTTTCCC 3' (SEQ ID NO:438)

Colonies of *E. coli* LE392 were picked onto a master plate of LB + 13 µg/ml chloramphenicol (incubate throughout the day at 37° C) and then into 50 µl H₂O which has been placed into a 96-well plate. 1 µl of this dilution was used in above PCR reaction
10 (if the 96-well dilution plate is kept you will not need to prepare a master plate). Cultures for minipreps of plasmid candidates may be prepared directly from the cell dilutions.

The PCR program was run (95 °C - 5 minutes, 30 Cycles of: 95 °C - 1 minute, 58 °C - 1 minute, 72 °C - 30 seconds, 72 °C - 10 minutes, 4 °C - hold).

15

A 10 µl/ reaction was run on a 1.0 % TBE gel. A gel designed for 96 well plates and a multichannel pipettor were used to ease loading of the sample rows. The gel was run and stained with ethidium bromide. The positive clones were identified with appropriate molecular size insert(s), amplified by the flanking pEVP-3 primers.

20

Minipreps Of Plasmids To Identify Cells Carrying The Pevp-3 Vector With An Insert

The constructs that carried an insert were identified. The constructs having an insert were inoculated into a 5 ml LB/Cm culture, and incubated over night at 37 °C with
25 aeration. Miniprep plasmid DNA was prepared by a standard procedure. The miniprep DNA was digested with appropriate restriction enzymes to confirm the presence of the insert (enzymes flank SmaI site in pEVP-3) (10 µl miniprep DNA, 2 µl 10 × buffer, 1 µl XbaI, 1 µl XhoI, 6 µl ddH₂O; 20 µl total volume for digest).

To confirm the presence of an insert, the digest reactions were electrophoresed on an agarose gel and the gel was stained with ethidium bromide. The positive clones were used for the *S. pneumoniae* KNOCKOUTs procedure.

- 5 The confirmatory PCR reactions, using knock out-specific primers (quality control step) involved 35.5 μ l H₂O, 5 μ l 10 \times Vent™ buffer, 1 μ l knockout forward primer (0.5 μ g/ μ l), 1 μ l knockout reverse primer (0.5 μ g/ μ l), 0.5 μ l Vent™ (6.0 μ l total) DNA Polymerase (2000 U/ml), 1.5 μ l each dNTPs (10mM, 6.0 μ l total), 1.0 μ l miniprep DNA from test
10 minutes, 30 Cycles of: 95 °C for 1 minute, 60 °C for 1 minute, 72 °C for 30 seconds, 72 °C for 10 minutes, hold at 4 °C. The presence of the correct-sized insert was confirmed by agarose gel electrophoresis and ethidium bromide staining. The confirmed clones were used for the *S. pneumoniae* gene KNOCKOUT procedure. Glycerol stocks were made of all positive *E. coli* LE392 constructs and frozen at - 80 degrees C.

15

EXAMPLE 3

- The following provides a description of the high throughput gene disruption procedure used in *S. pneumoniae* strain (e.g., gene knockout procedure). The candidate *ceg*
20 fragments that were generated by the method described in Example 2 were used in the gene disruption procedure in order to identify *ceg* nucleotide sequences that are required for cell viability.

- Reactions were set up in a 1.5 ml eppendorf tubes or 96 well plate (1 μ g total of miniprep
25 pEVP-3 + insert DNA (usually 10 μ l of Qiagen miniprep DNA); then 200 μ l of *S. pneumoniae* (strain Rx-1) competent cells diluted 1:10 in competence media was added (1 ml of competence media = 980 μ l Todd Hewitt (Difco Laboratories) with 0.5% yeast extract, 20 μ l 10% BSA, 1 μ l 10 % CaCl₂, and 0.5 μ l (200 μ g/ml) Csp-1 competence peptide).

30

Controls were run with each KNOCKOUT experiment and involved 1 µg pEPV3 *Lyt A* construct = positive control (non-essential), or 1 µg pEPV3 *Fts Z* construct = negative control (essential). Then the 96 well plates and controls were incubated at 37 °C for 2.5 to 3 hours in 37 °C room without shaking. The 200 µl of the samples were plated on
5 Todd Hewitt agar plates with 0.5% yeast extract and 2 µg/ml chloramphenicol.

The samples were incubate over night at 37 °C in 5% CO₂ incubator. Control plates were checked for presence of colonies (pEVP-3::*lytA*) and no growth (pEVP-3::*ftsZ*). Plates were examined for growth (ca. 70-150 colonies) designating nonessentials and zero
10 colonies designating essential genes.

The polarity test was performed in a similar manner, using the polarity fragments described in Example 3.

15

EXAMPLE 4

The following provides a description of the autolysin procedure used to determine that the non-essential control samples of *S pneumoniae* contain a disrupted *lytA* gene.

20

Phenotypic Autolysin Test

The culture plates containing transformants carrying the *lytA* control vector were flooded
25 with 0.1% deoxycholate in H₂O. The plates were observed after 5-10 minutes. Plates with "ghosts" indicated intact *lytA* gene, or plates without "ghosts" indicated a disrupted *lytA* gene. The "ghost" phenomenon is due to detergent triggered autolysis of the cells, causing a gradual fading of the colonies.

30 The detergent treatment triggers the autolysin in *lytA* intact cells; it cannot trigger the autolysin (*lytA* gene product) in *lytA* disrupted cells. Colonies with intact *lytA* "ghost" in 5-10 minutes due to massive pneumococcal cell lysis.

EXAMPLE 5

The following provides a description of the procedure used to express the CEG proteins (e.g., designated CFE proteins) in *E. coli* cells.

CEG Protein Production

Full-length *ceg* gene were inserted into pET-21 expression vector using the *E. coli* BL21 λ DE3 expression system using the following method:

For each *ceg*, custom primers were used to insert N- and C- termini into vectors such that the 5' end (N-terminus of the CEG) is positioned properly for expression behind the T7 promoter and optimally placed with regard to the pET ribosome binding site. The pET vectors contain an *NdeI* site which allows positioning of ATG start site in the vector. In cases where the *ceg* sequence contains an internal *NdeI* site, blunt ligation of the *ceg* PCR fragment into the vector is accomplished via Klenow fill-in of the *NdeI* site. In many cases, primers were also designed such that the *ceg* 3' (C-terminus of the expressed protein) will contain an in-frame extension of 6X-histidine residues, encoded in the vector sequence of pET-21. The individual *cegs* were PCR amplified via custom designed primers as described above. Both *ceg* PCR and vector DNA were digested with appropriate restriction enzymes. The full-length *ceg* were ligated into the pET expression vector. The ligation mixture was transformed into competent *E. coli* BL21 λ DE3 cells and selected for transformants on LB agar with 50 μ g/ml ampicillin. Positive insert bearing clones were screened via minipreps of the plasmids and size analysis on 0.8% agarose gels, with detection by ethidium bromide staining, as above.

Protein Production

The proper reading frame of each *ceg* inserted into pET-21 is verified by DNA sequencing.

A small (2-5 ml) test culture of *E. coli* BL21 λ DE3 with the insert-bearing plasmid is tested for protein expression by IPTG induction of the expression vector for 1-2 hours. The expression is verified by SDS-Polyacrylamide Gel Electrophoresis analysis of a whole cell extract (SDS extract of 0.5-1 ml of cells treated at 100 °C for 5 minutes) to determine whether the protein is over-expressed and migrates at the correct predicted molecular weight.

The protein is overproduced and purified via the following method. A large scale (500-1000ml) culture of *E. coli* is grown to early logarithmic phase in broth (e.g., LB broth) and protein expression induced for 2 hours with IPTG (isopropyl-D-thiogalactoside). The cells are harvested by centrifugation (8000 X G; 15 minutes) and the cell pellets resuspended in 20 ml. of buffer. The cells are lysed by sonication, and the supernatant fluid centrifuged at low speed (5000 X G, 15 min.) to remove unbroken cells. The supernatant fluid, containing the over-expressed protein is subjected to Ni-NTA affinity column chromatography (Quiagen, Inc., Chatsworth, CA). The 6X-histidine residues linked at the C-terminal end of the CEG proteins permit rapid protein purification via selective binding to a Ni-NTA resin column. The protein-bound Ni-NTA resin was to remove contaminants, and the bound proteins subsequently eluted with imidazole and recovered. It is possible to upscale this procedure to larger volumes for higher yields of proteins.

EXAMPLE 6

The following provides a description of the methods used to purify all 2CEG polypeptides (e.g., 2CFE polypeptides #19-117; SEQ ID NOS:349-436) having a histidine tag at their C-terminal ends. The 2CEG polypeptides having the his-tags were produced by the methods described in Example 5, *supra*. As an example, results of purification of 2CFE 75 polypeptide are presented.

Production Of The CFE Polypeptides

The BL21λDE3 cells harboring recombinant pET-21 vectors carrying a 2CFE nucleotide sequence (SEQ ID NOS:244-331) were cultured in LB broth containing ampicillin.

- 5 When the A_{600} reached approximately 0.6, protein production was induced by adding 1.0 mM of IPTG, the cells were cultured for an additional 2 hours. The cell pellet was collected by centrifugation, and the collected cell pellet was sonicated in Solution A (50 mM NaPO_4 , 300 mM NaCl, pH 8.0). The sonicated cells were centrifuged at 10,000 RPM to remove the debris.

10

Purification Of The CFE Polypeptide

The supernatant was diluted with Solution A, loaded onto a Ni-NTA column (Quiagen) equilibrated with Solution A; the column bed size was 2.5 x 25 cm, and the flow rate was
15 approximately 3.0 ml/minute. The 2CFE protein was eluted using a linear gradient of imidazole, using 0-250 mM in 450 ml, flow rate approximately 3.0 ml/minute. The eluted samples were collected as 22 ml fractions per tube and the eluted samples were monitored using spectrophotometry. The amount of protein in the eluted fractions was estimated using the Bradford method (Bradford, M. M., 1976 *Anal. Biochem.* 72:248) and
20 the samples were run on an SDS-PAGE gel (Novex EC6008) (Figure 3 A). Fractions were selected for pooling based on the results of the SDS-PAGE gel. The pooled fractions were concentrated using a 10,000 MW Centricon (Amicon) to approximately 5 ml.

- 25 The 2CFE 75 polypeptide, a precipitate formed and was redissolved upon increasing the sample volume and removing the imidazole by repeated concentration in 50 mM Tris, 100 mM NaCl, pH 7.5. Varying amounts of the 2CFE 75 polypeptide were diluted in either 20 mM Tris, 20 mM KCl, pH 7.5 or 20 mM Tris, 20 mM MgCl_2 , pH 7.5 at concentrations of 12, 24, or 36 ug/ml. The diluted samples were electrophoresed on an
30 SDS-PAGE gel under non-reducing conditions (Figure 3 B). The results of Figure 3 B suggests that 2CFE 75 forms a multimer.

EXAMPLE 7

The following provides a description of the methods used to purify CEG polypeptides that lack a histidine tag (e.g., 2CFE polypeptides #1-17; SEQ ID NOS:332-348). As an example, the results of purification of CFE 3 polypeptide are presented.

Purification of the CFE 3 Polypeptide

The 2CFE 3 polypeptide was produced using the large scale IPTG-induced method described in Example 5, *supra*. The 2CFE 3 (SEQ ID NO:334) polypeptide lacks a C-terminal histidine tag. The 2CFE 3 polypeptide was purified using a 2-column procedure. The 2CFE 3 polypeptide preparation was eluted from a 26/10 Q Sepharose column (Pharmacia) using a 0-1.0 M NaCl gradient, 2 ml/minute flow rate, and the gradient size was 1 liter. Then the 2CFE 3 polypeptide was eluted from a hydroxyapatite Bio-gel column (Bio-Rad) using a 5-200 mM potassium phosphate (pH 8.0) gradient, the flow rate was 0.3 ml/minute, and the gradient size was 300 ml. A sample of the 2CFE 3 preparation was run on a polyacrylamide gel (Figure 4).

EXAMPLE 8

The following provides a description of the size exclusion chromatography methods used to estimate the molecular weight and determine whether the CEG polypeptides oligomerize. The CFE polypeptide may oligomerize to form monomers, dimers, tetramers, hexameric rings, or other oligomeric forms.

Size exclusion chromatography was performed on all isolated 2CFE polypeptides #s 1-117 (e.g., SEQ ID NOS:332-436). This method was performed using various types of columns, depending on the particular 2CFE polypeptide tested.

The Biosil SEC-125 HPLC Gel Filtration column (BioRad Laboratories, Inc) was used, for example, to characterize CFE 8. The mobile phase was 0.2 M KH_2PO_4 , 0.9% NaCl pH 6.8.

- 5 The Phenomenex 600 x 7.5 mm Biosep SECS 3000 column was used, for example to characterize 2CFE 21 and 39. The mobile phase for size exclusion was 50 mM Na_2HPO_4 , pH 7.0 and 150 mM NaCl run at 1 ml/minute in a Gilson HPLC system, with protein detection at 280 nm.

10 EXAMPLE 9

The following provides a description of the computer-aided methods used to search for similarities between the amino acid sequences of the CEG polypeptides and sequences available through public and proprietary databases. In many cases, the function of the
15 CEG polypeptides was suggested by the results of the similarity searches. The function of some of these CEG polypeptides has been confirmed by performing additional analyses. Table V provides a list of the suggested and confirmed functions of CEG polypeptides designated CFEs #1-117.

- 20 The putative function of the CFE polypeptides were determined using computer-aided bioinformatic approaches, including distant homologies, motif searching, or predictions based on statistical rules. For example, the distant homology approach involved pairwise or multiple sequence alignments, employing tools such as FASTA, and Psi-BLAST. The motif searching approach involved using sophisticated hidden Markov models. The
25 approach based upon predictions of statistical rules involved prediction of transmembrane regions, coiled-coil, and other structural motifs. These approaches have been reviewed in *Computational Methods In Molecular Biology* 1998, eds. Salxber, S.L., Searls, D.B. Searls, and Kasif, S. , Elsevier, and in *Bioinformatics: A Practical Guide To The Analysis Of Genes And Proteins* 1998 eds Baxevanis, A. D. and Francis Ouellete, B.F. , Wiley-Interscience.

30

Global sequence similarity searches were performed using the amino acid sequences of all the conserved essential gene sequences (e.g., CFEs 1-117; SEQ ID NOS:114-226) to search against a non-redundant protein database using the BLAST2 algorithm (Altschul S.F., et al., 1997 *Nucleic Acids Res.* 25(17):3389-3402). In a similar search, similar
5 sequences were identified in the Concordance database using the "Neighbor" function (Brucoleri R. E., Dougherty T.J., Davison D.B. 1998 *Nucleic Acids Res.* 26(19):4482-4486). To determine if the predicted amino acid sequences were full length and in the proper reading frame, BLAST-type searching and CLUSTAL multiple sequence alignments (Higgins D.G., et al., 1996 *Methods Enzymol.* 266:383-402) were used.
10 Local sequence similarity searches were performed, by searching for Prosite (Hofmann K., et al., 1999 *Nucleic Acids Res.* 27(1):215-219) and Pfam motifs (Bateman A., et al., 2000 *Nucleic Acids Res.* 28(1):263-266). Additionally, the amino acid sequences of the CFEs were analyzed by performing protein threading analyses using the ProCeryon fold recognition program (Sippl, et al., 1992 *Proteins* 13:258-271; Sippl, J. 1993 *J. Comp.*
15 *Aided Mol. Design* 7:473-501; www.proceryon.com) and Geneformatics.

In bacteria, many operons include genes encoding different proteins that catalyze discrete steps of a common biochemical pathway. Therefore, the operon structures in *S. pneumoniae* was compared with that in other bacteria in order to predict the function of
20 CFE polypeptides.

Additionally, analysis of bacterial metabolic pathways were performed using Pathway Tools from DoubleTwist, based on the EcoCyc system (Karp P.D., et al., 1999 *Nucleic Acids Res.* 1999 27(1):55-58). This analysis was used to predict which CFEs mediate
25 various steps of the pathways.

When the sequence identity between a CFE polypeptide and the annotated database (e.g., SwissProt, Genbank) was low (e.g., sequence identity less than about 30%), a Protein Threading (e.g., fold recognition) method was used to predict similarities in the folded
30 protein structure of CFE polypeptides in the absence of a high level of sequence similarity with proteins in the databases (review by Teichmann, et al., 1999 *Current Opinion in*

Structural Biology 9:390-399). The Protein Threading method predicts the compatibility of a query sequence (e.g., CFE polypeptide sequences) with each of the folds in a library of known protein structures. The library of known protein structures as developed, maintained, and updated throughout the search process.

5

A list of potential structural folds, onto which each query was compatible, was generated for all CFE polypeptides (e.g., SEQ ID NOS:114-226). The fold assignments for each query were used to generate pairwise sequence alignments. The pairwise sequence alignments were used to generate protein models of the query polypeptide (e.g., CFE polypeptides).

10

The pairwise sequence alignments were also used to compare the position of critical residues of the structural template with the query polypeptide. The list of critical residues was generated by using multiple sequence alignments derived from a structural classification of proteins to generate a conservation profile which provided sequence-specific positions conserved across a homologous family of protein folds. Comparative modeling was used to search the model of the query polypeptide for the critical residues and determine whether the structural and functional motifs are conserved in the query protein. Conservation of structural and functional motifs permitted assignment of putative structure and function to a query polypeptide sequence.

20

The Protein Threading method was used to search for putative folded structure and function for all CFE polypeptides (SEQ ID NOS:114-226). The CFE polypeptides having significant sequence identity (e.g., more than 30%) to known proteins were assigned putative functions with a high level of confidence.

25

EXAMPLE 10

The following provides a description of the methods used to characterize purified, CFE 101 polypeptide. The 2CFE 101 polypeptide mediates the conversion of pantothenate to 4' phosphopantothenate, and is predicted to be a pantothenate kinase.

30

Computer-Aided Comparison

The computer-aided comparison, as described in Example 9 *supra*, suggests that the amino acid sequence of the CFE 101 polypeptide (SEQ ID NO:210) is 42% similar to the amino acid sequence of the coaA protein of *E. coli*. Thus, CFE 101 may be a pantothenate kinase, which mediates the conversion of pantothenate to 4' phosphopantothenate (Figure 5).

Circular Dichroism and Circular Dichroism Thermal Melt Analysis

Circular dichroism and circular dichroism melt methods were used to determine the folded structure of the expressed and isolated 2CFE polypeptides. For example, this method was used to characterize the folded structure of isolated 2CFE 101 (SEQ ID NO:421).

The starting concentration of the 2CFE 101 polypeptide was such that OD₂₀₅ was approximately 1.5, and the OD₂₈₀ was approximately 0.05 (e.g., 0.05 to 0.1 mg/ml). The starting concentration of 2CFE 101 was approximately 344 μ M in 50% glycerol, 50 mM Tris, 100 mM NaCl, 5 mM MgCl₂, 0.5 mM EDTA, at pH 7.5. The polypeptide was diluted to a final concentration of 7 μ M, as determined by absorbance at A₂₈₀, in 20 mM Na-phosphate, 100 mM KCl, at pH 7.0. The circular dichroism analysis was performed using quartz cuvettes, the instrumentation was from JASCO (Model J-720), the readings were performed at 25 degrees C (Figure 6 A). The band width was 1 nm, the sensitivity was 20 mdeg, the response was 0.25 seconds, the scan speed was 50 nm/minute, and the step was 0.5. The circular dichroism thermal melt analysis was performed at a range of between 0 and 100 degrees C (Figure 6 B). Additionally, the circular dichroism was performed comparing monomer and aggregate pools of 2CFE 101.

Size Exclusion Analyses

Size exclusion chromatography methods were performed using the Biosil SEC column, as described in Example 8 *supra*. The results suggest that the 2CFE 101 polypeptide forms monomer (40,200 Da) and oligomers (194,000 Da). The specific activity of the monomer and oligomeric forms of 2CFE 101 were determined, as described below.

Biochemical Assays

The biochemical assays of the 2CFE 101 polypeptide was based on the PK/LDH coupled enzyme assays described by Vallari, D. S., et al. (1987 *J. Biol. Chem.* 262:2468-2471) and Song, W. -J., et al., (1994 *J. Biol. Chem.* 269:27051-27058).

Briefly, the assay was performed as follows. The reaction included: 885 μ l of 0.1 M Tris-HCl (pH 7.6), 25 μ l NADH (14.1 mM), 20 μ l ATP (10.7 mM), 50 μ l phospho-enol-pyruvate (56 mM), 5 μ l LDH/PK (lactose dehydrogenase/PK; Sigma, catalog # P-0294, 60 U/ ml PK, 1050 U/ml LDH), 5 μ l of the 2CFE 101 polypeptide (9 mg/ml in 50 mM Tris-HCl, pH 7.5, 100 mM NaCl which was diluted to 4.5 mg/ml in 50% glycerol). The reaction was started by adding 10 μ l pantothenate (100 mM; Sigma, catalog # P2250). The production of ADP in the reaction was monitored by measuring the absorbance at 340 nm. The results in Figure 8 show that the 2CFE 101 polypeptide mediates ADP production in the presence of pantothenate and ATP. The K_m of pantothenate ($n=4$) was 144 (± 16.5) μ M, the V_{max} of the 2CFE 101 polypeptide ($n=4$) was 2.04 (± 0.25) μ M min^{-1} mg^{-1} . The monomer form has a specific activity of approximately 1.7 μ M min^{-1} mg^{-1} . The oligomeric form has a specific activity of 0.26 μ M min^{-1} mg^{-1} .

Alternatively, the 2CFE 101 polypeptide can be tested in an assay that monitors the conversion of pantothenate to 4'-phosphopantothenate. The same reaction described above can be used, except ^{14}C -labeled pantothenate is used. The reaction can be monitored by measuring the amount of ^{14}C -labeled 4'-phosphopantothanate produced.

EXAMPLE 11

The following provides a description of the methods used to characterize purified, CFE 39 and CFE 21 polypeptides, carrying a C-terminal histidine 6-tag. The methods include
5 helicase reactions, in which synthetic Holliday Junction templates are resolved into duplex structures. In one method, helicase reaction was monitored using radiolabeled templates. In another method, the helicase assay was adapted for use in a high throughput assay employing fluorescence labeled templates.

10 Computer-Aided Comparison

The computer-aided comparison, as described in Example 9 *supra*, suggests that the CFE 39 polypeptide (SEQ ID NO: 148) is an RuvA homologue. The comparison also suggests that CFE 21 (SEQ ID NO:132) is an RuvB homologue.

15

Previous studies by Parsons and others have shown that RuvA and RuvB proteins, in *E. coli*, promote branch migration or movement of Holliday Junctions during genetic recombination and DNA repair (Parsons, C. A., et al., 1992 *Proc. Natl., Acad. Sci. USA* 89:5452-5456; Tsaneva, I. R., et al., 1993 *Proc. Natl., Acad. Sci. USA* 90:1315-1319;
20 Muller, B., et al., 1993 *J. Biol. Chem.* 268:17179-17184; Mitchell, A. H. and S. C. West 1996 *J. Biol. Chem.* 271:19497-19502; Parsons, C. A. and S. C. West 1993 *J. Molec. Biol.* 232:397-405; Tsaneva, I. R., et al., 1992 *Molec. Gen. Genet.* 235:1-10; Mitchell, A. H. and S. C. West 1994 *J. Molec. Biol.* 1994 243:208-215).

25 Size Exclusion Chromatography

Size exclusion chromatography was performed on 2CFE 39 (SEQ ID NO:366) and 2CFE 21 (SEQ ID NO:350) using the Phenomenex 600 x 7.5 mm Biosep SECS 3000 column, as described in Example 8 *supra*. Protein standards (BioRad) were used to calibrate the
30 column, including thyroglobulin (670,000 Da), gamma globulin (158,000 Da), ovalbumin (44,00 Da), myoglobin (17,00 Da), and B-12 (1350 Da).

The results indicate that 2CFE 39 (RuvA) forms tetramers and 2CFE 21 (RuvB) forms a hexameric ring structure. Selected eluted samples were electrophoresed on a polyacrylamide gel (Novagen) (Figure 9).

5

The Holliday Junction Analysis Using Radiolabeled Templates

The Holliday Junction analysis was performed using radiolabeled, synthetic, asymmetrical, Holliday Junction templates, as described in Hiom, K. and S. C. West
10 1995 *Cell* 80:787-793. The Holliday Junction templates were produced by annealing together four separate, single-stranded, oligonucleotide strands to form four-stranded structures (e.g., the Holliday Junction template). The Holliday Junction templates were reacted with the 2CFE 39 and 2CFE 21 polypeptides, in a helicase reaction, to test their ability to generate two duplex structures.

15

Producing the Synthetic Holliday Junction Templates

The asymmetrical Holliday Junction templates were produced by annealing the following oligonucleotide sequences:

20

Oligonucleotide strand 1:

5'-CCAGTGATCACATACGCTTTGCTAGGACATCTTGATATCAGCCCACGTT
CACCCGCCTACCAGTGCCACGTTGTATGCCACGTTGACC-3' (SEQ ID NO:438)

25 Oligonucleotide strand 2:

5'-GGGTCAACGTGGGCATACAACGTGGCACTGGTAGGCGGGTGAACGTGGG
CTGATATCAAGATGTCCATCTGTCCGTTCTATGACGT-3' (SEQ ID NO:439)

Oligonucleotide strand 3:

30 5'-AACGTCATAGATGAACGGACAGATCATGGTGCTTTTAAAGTCTAGAGAC
TATCGAGCATTAGTACCAGTATCGAATCCGTCTTGTC-3' (SEQ ID NO:440)

Oligonucleotide strand 4:

5'-TTTGACAAGACGGATTTCGATACTGGTACTAATGCTCGATAGTCTCTAGAC
TTTAAAAGCACCATGTAGCAAAGCGTATGTGATCACTG-3' (SEQ ID NO:441)

5

Oligonucleotide strand 3 was labeled at the 5' end using approximately 300 ng of oligonucleotide strand 3, 1 μ l 10x Phosphate Buffer, 5 μ l 32 P ATP, 1 μ l T4 polynucleotide kinase (Gibco-BRL), in a 10 μ l volume, and the reaction was performed at 37 degrees C for 30 minutes. The reaction was loaded onto a G50 column to remove the
10 unincorporated radiolabel. The final concentration of the radiolabeled oligonucleotide strand 3 was approximately 15 ng per μ l.

Approximately equimolar amounts of the four oligonucleotide strands were annealed (e.g., hybridized). The annealing reaction included: 5 μ l Annealing Buffer (200 mM
15 Tris-Cl pH 8.0, 100 mM $MgCl_2$, 1 M NaCl, 10 mM DTT); 450 ng of radiolabeled oligonucleotide strand 3; and 1000 ng each of oligonucleotide strands 1, 2, and 4; in 50 μ l total reaction volume. The control annealing reaction included: 5 μ l Annealing Buffer, 60 ng radiolabeled oligonucleotide strand 3; 1000 ng oligonucleotide strand 4; in 50 μ l total reaction volume. Annealing was performed at 95 degrees C for 5 minutes, 65
20 degrees C for 30 minutes, 42 degrees C for 30 minutes, and room temperature (e.g., between about 23 to 27 degrees C) for 30 minutes to generate the synthetic Holliday Junction templates. The synthetic Holliday Junction templates were gel or column-purified to remove the duplex and non-annealed products. As a control, oligonucleotide strands 3 and 4 were annealed to form duplex structures. The synthetic Holliday Junction
25 templates and duplex structures were stored at -20 degrees C.

CFE 39 and CFE 21: The Helicase Reaction Using Radiolabeled Templates

The helicase reaction was performed to determine whether 2CFE 39 and 2CFE 21
30 resolved the synthetic Holliday Junction templates into duplex structures. The helicase reaction was performed as follows. A 50 μ l total reaction volume included: 25 μ l of 2x

Reaction Buffer (50 mM Tris-Cl pH8.0, 30 mM MgCl₂, 2 mM ATP); 1 µl synthetic Holliday Junction template (36 ng); 2 µl 2CFE 39 (1 µM); and 2 µl 2CFE 21 (1 µM). The reaction was incubated at 37 degrees for 30 minutes. The reaction was stopped by adding 5 µl Stop Buffer (100 mM Tris-Cl pH 7.5, 5 mg/ml Proteinase-K, 5% SDS). The stopped reaction was returned to 37 degrees C for 5 minutes. The helicase reaction was loaded onto and run on a non-denaturing, 12% PAGE, Tris-glycine gel.

The results shown in Figure 10, lanes 6, 7 and 8, indicate that the 2CFE 39 and 2CFE 21 polypeptides resolved the synthetic Holliday Junction templates into duplex structures.

CFE 39: The Helicase Reaction

It has been previously shown that *E. coli* RuvA binds to Holliday Junction templates (Parsons, C. A., et al., 1992 *Proc. Natl., Acad. Sci. USA* 89:5452-5456). The ability of *S. pneumoniae* CFE 39 to bind to a Holliday Junction template can be tested by employing the helicase assay described herein. The results of the helicase assay can be monitored by performing a gel shift assay and/or capillary electrophoresis. The presence of a Holliday Junction template bound to 2CFE 39, which migrates more slowly than the Holliday Junction template alone, would indicate that *S. pneumoniae* 2CFE 39 binds to Holliday Junction templates.

CFE 39 and CFE 21: Holliday Junction Analysis Using Fluorescent-Labeled Templates

The helicase reaction described herein was performed using Holliday Junction templates having one oligonucleotide strand labeled with a fluorescent agent and another strand labeled with a quenching agent. The 5' fluorescent end and the 3' quenching end of the strands that make up the Holliday Junction templates are in proximity to each other, resulting in a non-fluorescent template. When the Holliday Junction templates are resolved into duplex structures, the fluorescent and quench ends are not in proximity to each other, resulting in fluorescence.

The Holliday Junction templates used to perform this experiment comprised the following: the 5' end of oligonucleotide strand 1 was labeled with a fluorescein (e.g., the fluorescent agent), and the 3' end of oligonucleotide strand 4 was labeled with DABCYL (e.g., the quenching agent). The oligonucleotide strand 1 labeled with fluorescein and the oligonucleotide strand 4 labeled with DABCYL were custom synthesized (Gibco-BRL Life Technologies, Inc.).

The fluorescein and DABCYL labeled oligonucleotides were annealed in a reaction, as described above, to generate synthetic Holliday Junction templates. The helicase reaction was performed as described above. The results of the helicase reaction were monitored by measuring the unquenching of the Holliday Junction templates with time (Figure 11).

The helicase assay using Holliday Junction templates labeled with fluorescent-quenching agents can be adapted for use in high throughput analyses to test 2CFE 39, 2CFE 21, and other polypeptides for their ability to resolve the templates into duplex structures.

EXAMPLE 12

The following provides a description of the methods used to characterize purified, CFE 8 polypeptide, which lacks a histidine tag. The CFE 8 is a putative DNA single-stranded binding protein.

Computer-Aided Comparison

The computer-aided comparison, as described in Example 9 *supra*, suggests that the CFE 8 polypeptide (SEQ ID NO:121) may be a single stand binding protein homologue, such as SSB.

Size Exclusion Chromatography

The 2CFE 8 polypeptide (SEQ ID NO:339) was characterized by size exclusion chromatography, using the Biosil SEC-125 HPLC Gel Filtration column as described in Example 8 *supra*. The chromatogram showed one peak corresponding to a molecular weight of approximately 89 kDa. Based on the nucleotide sequence, the predicted molecular weight of 2CFE 8 is 17,351 Da. In non-denaturing conditions, 2CFE 8 forms a multimer.

10 Binding Reaction

The 2CFE 8 polypeptide was reacted with a single-stranded oligonucleotide A. Briefly, the binding reaction included: 50 μ M of 2CFE 8 polypeptide, 50 μ M oligo strand A, 20 mM Tris/20 mM KCl pH 7.5. The binding reaction was performed at 37 degrees C, for 2 hours.

Oligonucleotide strand A:

5'-TTAGGGCCCGGGCTATCTTACAATCTCGTT-3' (SEQ ID NO:442)

20 Capillary Electrophoresis

The results of the binding reaction was monitored by capillary electrophoresis, following the methods described in "Handbook of Capillary Electrophoresis" 2nd Edition, 1997, ed. J. Landers.

Separation was performed using an uncoated capillary tube (360 μ m o.d., 50 μ m i.d., with a 50 cm effective separation length; Watrex International, Inc., Pittsford, NY) and 50 mM borate pH 9.3 as the mobile phase, at 25 kVolts, 20 minutes separation time.

30 The results indicate that 2CFE 8 alone elutes as a sharp peak, indicating little adsorption to the uncoated capillary wall (Figure 12 A). The shape of the peak and peak retention

time changed with 2CFE 8 in the presence of all oligonucleotides tested (Figure 12 B). As a negative control, MurB polypeptide (Pucci, M. J., L. F. Discotto, and T. J. Dougherty 1992 "Cloning and Identification of the *Escherichia coli* murB DNA sequence, which encodes UDP-N-acetylenolpyruvoylglucosamine reductase" *J. Bacteriol.* 174:1690-1693) was reacted with the same oligonucleotides. MurB reacted with or without the oligonucleotides showed no change in peak shape or retention time.

After capillary electrophoresis analyses, the 2CFE8 alone and 2CFE plus oligonucleotide samples were run on native polyacrylamide gels to determine whether the polypeptide was intact. The results indicate that in all cases, 2CFE 8 was intact and had not degraded with time or storage.

Mobility Shift Assays

The ability of 2CFE 8 polypeptide to bind oligonucleotide strand A was tested in a mobility shift assay.

The results indicate that 2CFE 8 binds single stranded oligonucleotides (Figure 13 A and B). In Figure 13 A, the gel was stained with ethidium bromide. The unbound oligonucleotides appear near the bottom of the gel, while the bound oligonucleotides appear near the middle. The same gel was stained with Coomassie (Figure 13 B), revealing that 2CFE 8 polypeptide bound to the oligonucleotide migrated further than unbound 2CFE 8, due to the change in charge carried by the oligonucleotide. Various ratios of 2CFE8:oligo were tested. The optimal binding ratio was 2:1.

The Effect of MgCl₂

The 2CFE 8 polypeptide precipitated in the presence of 5 mM MgCl₂. The precipitation was reversible by the addition of 1 μ M of the oligonucleotides tested. The observation indicates specific binding between 2CFE 8 polypeptide and the oligonucleotides tested.

Scintillation Proximity Assay

Scintillation proximity assay (SPA) methods can be used in a high throughput screening procedure to monitor, for example, a binding reaction. SPA utilizes beads (Amersham) which are coated on the surface with a particular compound or molecule. For example, the SPA bead may be coated with avidin to facilitate binding with any molecule having a biotin tag.

The binding reaction of the 2CFE 8 polypeptide and the oligonucleotide strand A can be monitored using SPA beads and a scintillation counter. The beads can be coated with avidin, the 2CFE 8 polypeptide can be tagged with biotin, and the oligonucleotide strand A can be radiolabeled.

EXAMPLE 13

The following provides a description of the methods used to characterize purified, 2CFE 3 (SEQ ID NO:334) and 2CFE 86 (SEQ ID NO:409) polypeptides.

The 2CFE 3 polypeptide catalyzes the conversion of D-glucosamine-6-phosphate to D-glucosamine-1-phosphate, indicating that 2CFE 3 mediates amino-sugar biosynthesis through the N-acetyl glucosamine pathway (Figure 14).

The 2CFE 86 polypeptide catalyzes the conversion of D-glucosamine-1-phosphate to N-acetylglucosamine-1-phosphate, and the conversion of N-acetylglucosamine-1-phosphate to UDP-N-acetylglucosamine-1-phosphate, which indicates that 2CFE 86 also mediates amino-sugar biosynthesis through the N-acetyl glucosamine pathway (Figure 14).

Computer-Aided Comparisons Of CFE 3

The computer-aided comparison, as described in Example 9 *supra*, suggested that the CFE 3 polypeptide (SEQ ID NO:116) is a phosphoglucosamine mutase, such as GlmM.

Purification of the CFE 3 Polypeptide

The 2CFE 3 polypeptide was produced using the large scale IPTG-induced method described in Example 5, *supra*. The 2CFE 3 polypeptide lacks a C-terminal histidine tag.

5 The 2CFE 3 polypeptide was purified using a 2-column procedure. The 2CFE 3 polypeptide preparation was eluted from a 26/10 Q Sepharose column (Pharmacia) using a 0-1.0 M NaCl gradient, 2 ml/minute flow rate, and the gradient size was 1 liter. Then the 2CFE 3 polypeptide was eluted from a hydroxyapatite Bio-gel column (Bio-Rad) using a 5-200 mM potassium phosphate (pH 8.0) gradient, the flow rate was 0.3

10 ml/minute, and the gradient size was 300 ml. A sample of the 2CFE 3 preparation was electrophoresed on an SDS polyacrylamide gel (Figure 4).

Affinity Capillary Electrophoresis of CFE 3

15 Affinity capillary electrophoresis methods were used to determine whether the 2CFE 3 polypeptide binds to various glucose derivatives. Binding was performed under equilibrium conditions, in which the sugars were dissolved in the running buffer and reacts with 2CFE 3 during separation in the column. The affinity capillary electrophoresis method used to analyze 2CFE 3 follows the methods described in

20 "Handbook of Capillary Electrophoresis" 2nd Edition, 1997, ed. J. Landers.

Briefly, 2CFE 3 polypeptide was reacted with increasing amounts of various glucose derivatives (e.g., substrate) at 25, 30 and 37 degrees C. The glucose derivatives included UDP-glucose, glucose-1-phosphate, glucose-6-phosphate, glucosamine-1-phosphate, and

25 glucosamine-6-phosphate. The reaction included: 2CFE 3 polypeptide (2.0 mg/ml), separation buffer (25 mM Tris; 192 mM Glycine, pH 8.0; BupH Tris-Glycine Buffer Packs, Pierce). Separation was performed at 25 kVolts, separation time was 15 or 20 minutes.

30 The results shown in Figure 15 A indicate that at 25 degrees C, 2CFE 3 binds to D-glucose-1-phosphate in a dose-dependent manner, as the peak shape and/or the retention

time for 2CFE 3 changes in the presence of 100 and 500 μ M D-glucose-1-phosphate compared to unreacted 2CFE 3.

5 The results shown in Figure 15 B indicate that at 25 degrees C, 2CFE 3 binds to D-glucosamine-6-phosphate in a dose-dependent manner, as the peak shape and/or the retention time for 2CFE 3 changes in the presence of 100 and 500 μ M D-glucosamine-6-phosphate compared to unreacted 2CFE 3.

10 The results shown in Figure 15 C indicate that at 25 degrees C, the 2CFE 3 polypeptide also binds to glucose-6-phosphate.

15 A comparison of 2CFE 3 reacted with various glucose derivatives, at 30 degrees C, is shown in Figure 15 D. The results indicate that D-glucosamine-6-phosphate is a putative substrate for 2CFE 3, as this reaction exhibits the greatest change in peak shape and/or retention time.

CFE 3: Capillary Electrophoresis and Laser-Induced Fluorescence

20 In a further analysis of 2CFE 3 polypeptide, capillary electrophoresis was performed with laser-induced fluorescence in order to separate and detect interaction between the substrate (e.g., D-glucosamine-6-phosphate) and the product (e.g., D-glucosamine-1-phosphate) in a one dose, one time-point procedure.

25 The 2CFE 3 polypeptide was derivitized by reacting 10 mM FITC (fluorescein isothiocyanate dissolved in methanol; Calbiochem, San Diego, CA) with D-glucosamine-6-phosphate, at ambient temperature, in the dark, overnight. The FITC-derivatized 2CFE 3 polypeptide (2.0 mg/ml) was reacted with the substrate (D-glucosamine-6-phosphate and D-glucosamine-1-phosphate) for one hour.

30 Separation was performed using an uncoated capillary (360 μ m o.d., 50 μ m i.d., with a 50 cm effective separation length) and 50 mM borate (pH 9.3) as the mobile phase. The

argon-ion laser had an excitation wavelength of 488 nm and an emission filter of 520 nm (Beckman, Fullerton, CA). The results shown in Figure 16 indicate that 2CFE 3 binds and catalyzes the conversion of D-glucosamine-6-phosphate to D-glucosamine-1-phosphate.

5

Computer-Aided Comparison Of CFE 86

The comparison results, as described in Example 9 *supra*, suggested that the CFE 86 polypeptide (SEQ ID NO:195) is an acetyltransferase, such as GlmU which is a
10 bifunctional enzyme in *E. coli*. It has been previously shown that, in *E. coli*, GlmU is a bifunctional protein having both the acetyltransferase and uridylyltransferase active sites (Mengin-Lecreulx, D. and J. van Heijennort 1994 *J. Bacteriol.* 176:5788-5795; Gehring, Al., et al., 1996 *Biochemistry* 35:579-585). The bifunctional enzyme catalyzes the conversion of D-glucosamine-1-phosphate to N-acetylglucosamine-1-phosphate
15 (acetyltransferase), and catalyzes the conversion of N-acetylglucosamine-1-phosphate to UDP-N-acetylglucosamine-1-phosphate (uridylyltransferase). The K_m of the acetyltransferase and uridylyltransferase reactions has been previously calculated (Mengin-Lecreulx, D. and J. van Heijennort 1994 *supra*). Additionally, the crystal structure of GlmU from *E. coli* is known (Brown, K., et al., 1999 *EMBO J.* 18:4096-
20 4107).

Purification of the CFE 86 Polypeptide

The 2CFE 86 polypeptide (SEQ ID NO:409) has a C-terminal histidine tag. The 2CFE
25 86 polypeptide was produced using the large scale IPTG-induced method described in Example 5, *supra*. The 2CFE 86 polypeptide was purified using the Ni-NTA affinity column method described in Example 6, *supra*. The eluted 2CFE 86 polypeptide was dialyzed against 50 mM Tris-Cl, 100 mM NaCl, 25% glycerol, pH 8.0. Samples of the purified 2CFE 86 polypeptide were electrophoresed on a polyacrylamide gel (Figure 17).

30

Coupling CFE 3 and CFE 86 to Produce UDPAG

A biochemical assay was performed, to determine whether 2CFE 3 and 2CFE 86 convert D-glucosamine-6-phosphate to UDP-N-acetylglucosamine-1-phosphate (e.g., UDPAG).

- 5 The 2CFE 3 and 2CFE 86 polypeptides were used in a coupled reaction based on the assays described in Jolly, L. P., et al., 1999 *Eur. J. Biochem.* 262:202-210.

- A time-dependent and dose-dependent assay were performed. Briefly, the assay was performed in 96-well plates, each well including 100 μ l volume. The assay included: 1
10 mM D-glucosamine-6-phosphate (Sigma); 0.7 mM D-glucosamine-1,6-diphosphate (Sigma); 1.2 mM acetyl-Coenzyme A (Sigma); and 5 mM uridine-5'-phosphate (Sigma); 3 mM $MgCl_2$ (Sigma); 50 mM Tris-Cl, pH 8.0 (Life Technologies). The reaction was started by adding 1 μ g of 2CFE 3; and 10 μ g of 2CFE 86. The reaction was performed at room temperature. The reaction was stopped at 0, 15, 30, and 65 minutes, by filtering out
15 the 2CFE polypeptides.

- The results of the assay was monitored by HPLC (high pressure liquid chromatography) using an Optisil 10 μ SAX column (250 x 4.6 mm), measuring at 262 nm, the mobile phase was 150 mM KH_2PO_4 (pH 3.5), and 1.5 ml/minute flow rate. The results shown in
20 Figure 18 show the time-dependent assay and indicate that HPLC detected the presence of UDPAG.

CFE 86: The Uridylyltransferase Reaction

- 25 The 2CFE 86 polypeptide was tested in a uridylyltransferase reaction, in which N-acetyl-D-glucosamine-1-phosphate and UTP produce UDP-N-acetylglucosamine. The uridylyltransferase reaction was monitored using a malachite green/inorganic pyrophosphatase assay (e.g., malachite green-IPPAse assay) and/or monitored using HPLC. The malachite green-IPPAse assay was used to measure orthophosphate
30 production from digestion of the pyrophosphate liberated in the uridylyltransferase reaction.

The malachite green reagent was prepared as follows. A 0.045 % solution of malachite green (Sigma; M9636) was prepared in water. A 4.2 % solution of ammonium molybdate (Mallinckrodt) was prepared in 4N HCl. The malachite green and ammonium molybdate were mixed in a 3:1 ratio, and stirred for about 20 minutes. The mixture was filtered, and stored at 4 degrees C. The inorganic pyrophosphatase (Sigma; I-2267) was diluted to 0.1 U/ μ l in 50 mM Tris/3mM MgCl₂ pH 8.0, and stored at 4 degrees C.

The uridylyltransferase reaction was performed in 96-well plates. The coupled reaction described herein was performed, in the presence of 2CFE 3 alone or 2CFE 3 and 2CFE 86, and included the addition of 0.5 U/well of the diluted inorganic pyrophosphate. The reaction was mixed for 5 minutes at room temperature. The reaction was stopped by the addition of 240 μ l/well of the malachite green reagent and 30 μ l/well of 34% sodium citrate, and the reaction was mixed. The results of the uridylyltransferase reaction was monitored by spectrophotometry at 660 nm.

The results of separate uridylyltransferase reactions were monitored by HPLC, using a Phenosphere-NEXT C18 column (250 x 4.6 mm). The mobile phases included A and B as follows: A) methanol/10 mM potassium phosphate pH 6.5 (0:100); and B) methanol/10 mM potassium phosphate pH 6.5 (40:60). The mobile phases were run under the following conditions: 100% mobile phase A for 5 minutes, to 100% mobile phase B in 3 minutes; and hold 100% mobile phase B for 9 minutes. The retention time for the UDPAG product is approximately 5.75 to 6.0 minutes.

The results three uridylyltransferase reactions, monitored by HPLC are summarized in Table III below.

TABLE III

<u>Purified CFE 86:</u>	<u>Specific Activity (nmol/min/μg):</u>
2CFE 86-1	3.1
2CFE 86-2	3.4
2CFE 86-3	3.1

The results of the uridylyltransferase reactions, monitored by HPLC or HPLC and Malachite Green IPPase assays are summarized in Table IV below.

TABLE IV

<u>Reaction:</u>	<u>K_m (μM):</u>	<u>Method:</u>
<u>Acetyltransferase reaction:</u>		
Glucosamine-1-P	94	HPLC
Acetyl-coA	150	HPLC
<u>Uridylyltransferase reaction:</u>		
N-acetylglucosamine-1-P	48	HPLC and MG/IPPase
UTP	79	HPLC

EXAMPLE 14

The following provides a description of the methods used to characterize various 2CFE polypeptides, including CFE 21, 34, 35, 39, and 90. The molecular weight of these 2CFE polypeptides were analyzed by size exclusion chromatography and gel electrophoresis. The 2CFE 34, 35, and 90 polypeptides putatively mediate fatty acid biosynthesis.

Computer-Aided Comparison

The computer-aided comparison, as described in Example 9 *supra*, suggests that CFE 34 (SEQ ID NO:143), CFE 35 (SEQ ID NO:144), and 90 (SEQ ID NO:199) are polypeptides which mediate a fatty acid biosynthesis pathway (Figure 19)

The comparison suggests that CFE 34 is a malonyl CoA:ACP transacylase, which catalyzes the reaction in which malonyl CoA and acyl carrier protein (ACP) are converted to malonyl-ACP and CoA. Thus, the CFE 34 polypeptide may be a homologue of *E. coli* FabD.

The comparison suggests that CFE 90 is a 3-oxoacyl-ACP synthase II (beta ketoacyl-ACP synthase II) which catalyzes the reaction in which malonyl-ACP is converted to beta aceto acetyl-ACP. Thus, the CFE 90 polypeptide may be a homologue of *E. coli* FabF.

The comparison suggests that CFE 35 is a 3-oxoacyl-ACP reductase (beta aceto acetyl ACP reductase) which catalyzes the reaction in which beta-keto-acetyl-ACP is converted to beta-hydroxy-acetyl-ACP. Thus, the CFE 35 polypeptide may be a homologue of *E. coli* FabG.

Size Exclusion Chromatography

The estimated molecular weights of 2CFE 34 (SEQ ID NO:361), 2CFE 35 (SEQ ID NO:362), and 2CFE 90 (SEQ ID NO:413) were determined using the Biosil SEC-125 HPLC Gel Filtration column as described in Example 8, *supra*.

The results suggest that 2CFE 34 polypeptide is a monomeric protein (33,093 Da), 2CFE 35 is a trimeric protein (25,758 Da; approximately 85%), and 2CFE 90 is a dimeric protein (43,930 Da). Selected eluted samples of 2CFE 34 were electrophoresed on a polyacrylamide gel (Figure 20).

Biochemical Assay: CFE 34

The function of 2CFE 34 was determined by performing various biochemical reactions.

- 5 To determine whether 2CFE 34 catalyzes the conversion of malonyl-CoA to malonyl and CoA, the following reaction was performed.

The biochemical reaction was performed in the presence of acyl carrier protein. The reaction included the following: 10 μ M 14 C labeled malonyl-CoA, 20 μ M ACP, 30 μ M
10 2CFE 34 (e.g., FabD) in 20 mM Tris-Cl, pH 8.0 and 5 mM DTT in 300 μ l volume. The reaction was performed at room temperature (e.g., approximately 24 degrees C) for 30 minutes. The reaction was terminated with the addition of 45 μ l of 0.5% TFA. The labeled reaction was injected onto a MonoQ 5/5 column on a Gilson HPLC. Detection was performed by monitoring the radioactivity of the continuous flow-through of the
15 HPLC effluent. Chromatography was performed using a buffer gradient for column elution. Buffer A included 20 mM Tris-Cl, pH 8.3. Buffer B was the same as Buffer A and included 1 M NaCl. The program was held at 90% A, 10% B for 10 minutes followed by a linear ramp to a final mix of 50% of each Buffer A and B over 10 minutes.

- 20 The substrate (e.g., 14 C malonyl-CoA) eluted at 9.9 minutes, the product (e.g., 14 C malonyl-ACP) eluted at 14.3 minutes. The results indicate that CFE 34 catalyzes the conversion of malonyl-CoA and acyl carrier protein (ACP) to malonyl-ACP and CoA.

EXAMPLE 15

25

The following provides a description of the methods used to characterize CFE polypeptides 40, 41, and 46.

Computer-Aided Comparison

The computer-aided comparison, as described in Example 9 *supra*, suggests that the CFE 40 polypeptide (SEQ ID NO:149) is a phosphomethylpyrimidine (HMP-P) kinase
5 involved in thiamine biosynthesis.

The comparison, as described in Example 9 *supra*, suggests that the CFE 41 polypeptide (SEQ ID NO:150) has a GTP-binding motif and may be a protease.

10 The comparison, as described in Example 9 *supra*, suggests that the CFE 46 polypeptide (SEQ ID NO:155) has an ATP-binding motif.

Affinity Purification of CFE 41

15 The large-scale method described in Example 5 *supra* (e.g., IPTG-induced protein production) was used to prepare a sample of 2CFE 41 polypeptide (SEQ ID NO:368). The sample was affinity purified using the Ni-NTA method described in Example 6, *supra*. The eluted fractions were loaded onto and run on a 12% SDS-PAGE gel (Novex) (Figure 21).

20

Circular Dichroism and Circular Dichroism Thermal Melt Analysis

Circular dichroism and circular dichroism thermal melt methods were performed using JASCO instrumentation. The concentration of the isolated 2CFE 40 (SEQ ID NO:367)
25 was approximately 21 μ M, in a 0.1 cm pathlength cell at 210 nm. The circular dichroism spectrum suggests that this preparation of 2CFE 40 had mixed alpha and beta secondary structure. The circular dichroism thermal melt spectrum suggests that 2CFE 40 has a T_m of approximately 67 degrees C. The 2CFE 40 polypeptide precipitates at approximately the T_m .

The concentration of the isolated 2CFE 41 (SEQ ID NO:368) was approximately 70 μ M, in a 0.02 cm pathlength cell. The circular dichroism spectrum suggests that this preparation of 2CFE 41 had mixed alpha and beta secondary structure, with a greater percentage of alpha structures. The circular dichroism thermal melt spectrum suggests that 2CFE 41 has a T_m of approximately 38 degrees C. The 2CFE 41 polypeptide precipitates at approximately the T_m .

The concentration of the isolated 2CFE 46 (SEQ ID NO:373) was approximately 23 μ M, in a 0.1 cm pathlength cell at 280 nm. The circular dichroism spectrum suggests that this preparation of 2CFE 46 had mixed alpha and beta secondary structure. The circular dichroism thermal melt spectrum suggests that 2CFE 46 is highly stable at elevated temperatures. At 90 degrees C, the 2CFE 46 polypeptide exhibited only a 27% loss in signal and the polypeptide remained soluble.

Capillary Electrophoresis

Capillary electrophoresis was performed on samples of purified 2CFE 40, 41 and 46. The electropherograms of 2CFE 40, 41, and 46 are shown in Figure 22.

EXAMPLE 16

The following provides a description of methods that can be used to characterize CEG polypeptides (e.g., CFE polypeptides).

Computer-Aided Compilation

Computer-aided compilation of bacterial metabolic pathways may be analyzed using Pathway Tools from Doubletwise, based on the EcoCyc system (Karp P.D., et al., 1999 *Nucleic Acids Res.* 1999 27(1):55-58). This analysis may be used to predict which CFEs mediate various steps of the pathways. This information may be used in combination

with the results of a binding reaction which identifies a ligand or substrate that binds with a CFE polypeptide.

Identifying the Function of a CFE Polypeptide

5

The function of a CFE polypeptide may be identified by identifying a ligand or substrate which binds with the CFE polypeptide. The ligand or substrate may be identified using fractionation and affinity capillary electrophoresis methods. The following method is based upon the assumption that the bacterial cell lysate includes the ligand or substrate.

10

A bacterial host cells carrying an endogenous (e.g. native) CFE gene or carrying a recombinant vector which includes a CFE gene may be cultured so that the CFE polypeptide is produced by the cell. The cells may be ruptured in order to obtain the cell lysate. The cell lysate may be fractionated using HPLC technology. The HPLC fractions may be reacted with a CFE polypeptide in a binding reaction, and the binding reaction may be analyzed by affinity capillary electrophoresis methods. The ligand or substrate which reacts with the CFE polypeptide may be identified using mass spectrophotometry methods (in "Mass Spectrometry" 1990 eds. McCloskey, J. A., in *Methods in Enzymology* volume 193; Henion, J., et al., 1993 "Mass Spectrometric Investigations of Drug-Receptor Interactions" *Ther. Drug Monit.* 15:563-569; Loo, J. A., et al., 1999 "Application of Mass Spectrometry for Target Identification and Characterization" *Med. Res. Rev.* 19:307-319; Nguyen, D. N., et al., 1995 "Protein Mass Spectrometry: Applications to Analytical Biotechnology" *J. Chromatogr.* 705:21-45).

25 **EXAMPLE 17**

The following provides a description of nuclear magnetic resonance (NMR) spectroscopy methods that were used to characterize CFE polypeptides.

30 High resolution NMR spectroscopy was applied to ^{15}N -labeled, $^{13}\text{C}/^{15}\text{N}$ -labeled, $^2\text{H}/^{13}\text{C}/^{15}\text{N}$ -labeled, and type-specifically isotopically labeled CFE polypeptide samples

in the solution state for the following purposes: to assess various aspects of the structural state, e.g., foldedness, structural integrity; to refine a previously determined experimental structure of a close sequence homologue; to refine a homology-modeled structure; to assess the potential for a CFE polypeptide to bind small molecules; and to identify small-molecule pharmacophoric fragments that bind specifically to the CFE polypeptide ("Nuclear Magnetic Resonance" 1994 eds. James, T. L. in *Methods in Enzymology* volume 239).

The NMR analysis includes screening both a compound deck of approximately 4,500 commercially available, structurally and chemically diverse compounds (the small-molecule pharmacophore deck) and a compound deck of proprietary, known, anti-microbial compounds (anti-microbial deck) against the CFE polypeptides (i.e., target polypeptides) to determine, either based upon perturbations to the chemical shifts of the amide proton and/or nitrogen resonances, as measured from a two-dimensional proton-nitrogen heteronuclear single-quantum correlation spectrum (2D screening method), or based upon increases in the linewidth of the compound's proton resonance(s), as measured by a one-dimensional $T_{1\rho}$ spin-lock difference spectrum (1D screening method), both whether a compound binds to a CFE polypeptide and, in the case of the 2D screening method, where the compound binds on the CFE polypeptide.

Isotopic Labeling of CFE Polypeptides

BL21-DE3 *E. coli* bacteria are transformed with the CFE expression vectors. Expression takes place between 20°C and 37°C in minimal media containing [^{15}N]-ammonium sulfate as the sole nitrogen source and either glucose, [^2H] $_{13}$ -glucose, or [^{13}C] $_6$ -glucose as the sole carbon source. Glucose is used for preparing uniformly ^{15}N -labeled and $^2\text{H}/^{15}\text{N}$ -labeled CFE polypeptides. [^2H] $_{13}$ -glucose is used for preparing type-specifically $^1\text{H}/^{13}\text{C}$ -labeled, uniformly ^{15}N -labeled CFE polypeptides. [^{13}C] $_6$ -glucose is used for preparing $^{13}\text{C}/^{15}\text{N}$ -labeled CFE polypeptides. The minimal media is prepared in 100% H_2O for expressing both uniformly ^{15}N -labeled and uniformly $^{13}\text{C}/^{15}\text{N}$ -labeled CFE polypeptides; the minimal media is prepared in 95% D_2O (deuterium oxide) and 5% H_2O for expressing

both type-specifically $^1\text{H}/^{13}\text{C}$ -labeled, uniformly ^{15}N -labeled and just uniformly $^2\text{H}/^{15}\text{N}$ -labeled CFE polypeptides. In the case of type-specifically $^1\text{H}/^{13}\text{C}$ -labeled, uniformly ^{15}N -labeled CFE polypeptides, 40 mg/L of protonated and uniformly $^{13}\text{C}/^{15}\text{N}$ -labeled isoleucine, valine and leucine amino acids are added to the minimal media.

5

NMR Screening

Compounds in the anti-microbial deck are pre-dissolved to a target concentration of 16 mM in deuterated DMSO (dimethylsulfoxide) with each deck well containing only one
10 compound. Compounds in the small-molecule, pharmacophore deck are pre-dissolved in deuterated dmso to a target concentration of 50 mM in groups of 8, i.e., each deck well contains 8 unique compounds with each compound at a target concentration of 50 mM.

3.5 μl of compound is placed at the bottom of a well in a 96-well, screening plate. This
15 well will be referred to as the compound screening well. Each compound screening well contains solution from only one deck well. 166.5 μl of buffer is added to each compound screening well. 170 μl of a CFE polypeptide solution, initially at a concentration ranging from 200-300 μM , is added to each compound screening well; the contents of that well are then thoroughly mixed. The control screening well contains only 3.5 μl of deuterated
20 dmso. The screening plate is then centrifuged in a bucket rotor for 15 minutes at 3,500 rpm to insure that all particulate matter is at the bottom of the well.

The 2D screening method requires a single control screening well in which the compound solution consists only of deuterated DMSO. The 1D screening method requires a control
25 screening well for each compound screening well. In the case of the 1D screening method, the control screening well is prepared identically to the compound screening well except that the 170 μl of a CFE polypeptide solution is replaced by 170 μl of buffer.

The screening plate is covered with aluminum foil and placed onto a rack of a Gilson
30 liquid handler. The Gilson liquid handler, under computer control by the NMR host/data-acquisition software, is responsible for removing each sample from the screening plate,

injecting the sample into a high-resolution, $^1\text{H}/^{15}\text{N}$ double-resonance NMR flow-probe, removing the sample from the flow-probe, and dispensing it back into the screening plate well from which the sample was originally removed. NMR data are collected on the sample while the sample resides in the NMR flow-probe. The type of NMR data
5 collected depends upon whether the 2D or 1D screening method is being used.

Determining Structural Characteristics of a CFE Polypeptide

In assessing various aspects of the structural state of a CFE polypeptide, NMR was used
10 to provide the following information. The proton 1D spectra and proton-nitrogen 2D correlation NMR spectra were used to assess the overall foldedness of a CFE polypeptide without actually describing in detail that folded state. Unfolded and substantially misfolded proteins produced distinct signatures in these two types of NMR spectra.

15 The chemical shift of most protein nuclei in either the set $\{\text{H}_\text{N}, \text{H}_\alpha, \text{H}_\beta, \text{C}', \text{C}_\alpha, \text{C}_\beta, \text{N}\}$ or the set $\{\text{H}_\text{N}, \text{C}', \text{C}_\alpha, \text{C}_\beta, \text{N}\}$ for perdeuterated (e.g., ^2H -labeled) proteins were determined by procedures well known in the art that involve collecting up to 10 triple-resonance NMR data sets. The protein secondary structure was delineated as either helical, turn or extended (e.g., β -sheet) by measuring $\Delta(\delta_{\text{C}_\alpha} - \delta_{\text{C}_\beta})$, $\Delta\delta_{\text{C}'}$, and $\Delta\delta_{\text{H}_\alpha}$ where δ refers to the
20 chemical-shift value and Δ refers to the difference between chemical-shift values measured in this protein and those measured for the same residue type in a random-coil (unstructured), tetrameric peptide.

This secondary-structure profile was generated in approximately 2-3 weeks per protein.

25 The secondary-structure profile was used to confirm the functional identity of a protein. It was also used to refine the list of possible functional identities of folds, predicted by various computational techniques including fold recognition which is associated with a protein or polypeptide.

NMR was used to generate folds of proteins or polypeptides for which both no structure was known of a sequence homologue and no structural homologue was discernible in the PDB by fold recognition techniques.

5 Refining a Structural Model

Nuclear Overhauser (NOE) data were used to refine both homology-modeled structured and previously determined experimental structures of close sequence homologues. This process took approximately 2-3 weeks per structure.

10

The CFE 88 polypeptide was characterized by NMR analysis to establish its secondary structure. The NMR data was used to filter the computer-aided threading analysis. The NMR-determined secondary structure for CFE 88 suggested that CFE 88 is structurally similar to 4-aminoimidazole carboxylase.

15

The characteristics of other CFE polypeptides were analyzed by NMR methods. A computer-aided threading analysis revealed that the N-terminal domain of the protein EGA, which both binds and hydrolyzes GTP, was both structurally similar and sufficiently similar in sequence to CFE 52 to suggest that CFE 52 had a similar function.

20

The NMR data of CFE 103 suggests that this polypeptide is unfolded. Circular dichroism spectra, as a function of temperature, also indicated that CFE103 was unfolded.

The CFEs 2, 42, 43, 68 and 88 polypeptides were tested for their ability to bind potential inhibitor molecules by screening both the anti-microbial deck and the small-molecule, pharmacophore deck. CFE 34 was tested for its ability to bind potential inhibitor molecules by screening the anti-microbial deck.

25

Characterizing Small-Molecule Binding

NMR-based screening was used to measure binding against both the small-molecule, pharmacophore deck and the anti-microbial deck. Binding data from these screens
5 allowed assessment of the propensity of a protein to bind small molecules. The binding data was also used to identify sites on the protein which are capable of binding small molecules. The binding data was also used to identify common pharmacophores among the compounds which bind.

10 Reverse screening refers to a process whereby known anti-microbial compounds, the microbial target of which is unknown, are screened by a general method, e.g., binding as assessed by NMR, to find a physical interaction with polypeptide targets previously determined to be essential to the bacteria (i.e., the CFEs). The reverse screening method was used to determine which CFE polypeptides bind to which compounds in the anti-
15 microbial deck. The reverse screening method included the following. The compounds in a proprietary compound deck were screened for Minimal Inhibitory Concentration (e.g., MIC). The compounds exhibiting antimicrobial activity were designated active compounds. The CFE polypeptides were screened to determine which polypeptide bind to which active compounds. The CFE polypeptides which bound to the active
20 compound(s) were confirmed, where possible, i.e., in cases where an in-vitro assay was possible to construct, as being inhibited in their function as a polypeptide by the active compound(s) by examination of the inhibition profile of the compound(s) against the CFE polypeptides. For additional confirmation, the effect of the compound on the microorganism harboring the CFE polypeptide was monitored (e.g., whole cell assays).
25 The structure of the active compound was used as a basis to generate chemically-related compounds by iterative synthesis. The chemically-related compounds were tested in a screening assay for binding with CFE polypeptides. The active compounds and the chemically-related compounds of interest were the compounds which exhibited an increase in binding affinity for a CFE polypeptide and/or exhibited drug-like properties.

The results of the reverse screening are as follows. 127 compounds from the proprietary compound deck exhibited anti-microbial activity. 94 of these active compounds were selected based upon both lack of cytotoxicity and lack of excessive hydrophobicity. These 94 compounds were soluble to 16 mM in deuterated DMSO; these compounds were also deemed to be sufficiently soluble in aqueous buffer for both the 2D and 1D NMR screening methods.

This subset of 94 compounds was used in an NMR-based screen to determine which compound binds to which CFE polypeptide. The CFE 42 polypeptide bound two different compounds with K_d 's in the range of 0.2 to 1 mM; the CFE 43 polypeptide bound one compound with $K_d \sim 30$ -50 μ M; the CFE 34 polypeptide bound 13 compounds, one of which inhibited the polypeptide function with $IC_{50} < 10 \mu$ M.

The enzyme assay used to confirm the NMR results which suggested CFE 34 interaction with the compounds included the following: 10 μ M 14 C-labeled malonyl CoA; 20 μ M ACP, 30 pM CFE 34; 20 mM Tris-Cl, pH 8.0; 5 mM DTT; in the presence of absence of 50 μ M of a compound solubilized at 40 mM in 100% DMSO and dilute 100-fold into 10% DMSO and further diluted 8-fold for a final concentration of 50 μ M in 1.25% DMSO. The reaction was performed at room temperature, the reaction was stopped with the addition of TFA. Two hundred μ l of the reaction was injected onto a Mono Q 5/5 column. The chromatography conditions included: A) 20 mM Tris-Cl, pH 8.3; B) 20 mM Tris-Cl, pH 8.3, 1 M NaCl. Hold 10% B for 5 minutes, linear gradient from 10% B to 50%B in 10 minutes, back to 10% B in 1 minute, hold for 14 minutes to re-equilibrate. The reaction substrate (14 C- malonyl CoA) eluted at 9.9 minutes, the reaction product (14 C-malonyl ACP) eluted at 14.3 minutes.

What is claimed is:

1. An isolated nucleic acid molecule encoding a polypeptide which is (1) essential for the viability of a bacterial cell and (2) has at least any one of the functions of a pantothenate kinase, a Holliday Junction branch migration protein, a single stranded DNA binding protein, a phosphoglucosamine mutase, an acetyltransferase, an uridylyltransferase, a malonyl CoenzymeA:ACP transacylase, a 3-oxoacyl-ACP synthase II, a 3-oxoacyl-ACP reductase, a phosphomethylpyrimidine (HMP-P) kinase, a GTP binding protein, a ATP binding protein, or a 4-aminoimidazole carboxylase.
2. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:97 or Figure 115 and wherein the polypeptide is a pantothenate kinase.
3. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:35, Figure 60, SEQ ID NO:19, or Figure 44, and wherein the polypeptide is a Holliday Junction branch migration protein.
4. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:8 or Figure 33 and wherein the polypeptide is a single stranded DNA binding protein.
5. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:3 or Figure 28 and wherein the polypeptide is a phosphoglucosamine mutase.
6. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:82 or Figure 103 and wherein the polypeptide is an acetyltransferase.

7. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:82 or Figure 103 and wherein the polypeptide is a uridylyltransferase.

5 8. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:30 or Figure 55 and wherein the polypeptide is a malonyl CoenzymeA:ACP transacylase.

10 9. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:86 or Figure 107 and wherein the polypeptide is a 3-oxoacyl-ACP synthase II.

15 10. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:31 or Figure 56 and wherein the polypeptide is a 3-oxoacyl-ACP reductase.

20 11. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:36 or Figure 61 and wherein the polypeptide is a phosphomethylpyrimidine (HMP-P) kinase.

12. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:37, Figure 62, SEQ ID NO:48, or Figure 73, and wherein the polypeptide is a GTP binding protein.

25 13. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:42 or Figure 67 and wherein the polypeptide is a ATP binding protein.

14. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:84 or Figure 105 and wherein the polypeptide is a 4-aminoimidazole carboxylase.
- 5 15. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:48 or Figure 73 and wherein the polypeptide is a GTP binding protein.
- 10 16. An isolated nucleic acid molecule encoding a polypeptide which is essential for the viability of a bacterial cell, the nucleic acid molecule comprising a sequence shown in any one of SEQ ID NOS:1-113.
- 15 17. An isolated nucleic acid molecule encoding a polypeptide which is essential for the viability of a bacterial cell, the nucleic acid molecule comprising a sequence shown in any one of Figures 26-130.
18. An isolated nucleic acid molecule encoding any one of a polypeptide designated CFE 1-117 having the amino acid sequence shown in SEQ ID NO:114-226.
- 20 19. An isolated nucleic acid molecule comprising a nucleotide sequence which is complementary to the nucleotide sequence of claim 1, 16, 17 or 18.
20. The isolated nucleic acid molecule of claim 1, 16, 17 or 18 which is DNA or RNA.
- 25 21. The isolated nucleic acid molecule of claim 20, which is labeled with a detectable marker.
- 30 22. The isolated nucleic acid molecule of claim 21, wherein the detectable marker is selected from the group consisting of a radioisotope, a fluorescent compound, a

bioluminescent compound, a chemiluminescent compound, a metal chelator and an enzyme.

23. A vector comprising the nucleotide sequence of claim 1, 16, 17, or 18.

24. A host-vector system comprising the vector of claim 23, in a suitable host cell.

25. The host-vector system of claim 24, wherein the suitable host cell is selected from a group consisting of a yeast cell, a plant cell, and an animal cell.

26. The host-vector system of claim 24, wherein the suitable host cell is selected from a group consisting of an *Escherichia* cell, a *Bacillus* cell, a *Pseudomonas* cell, a *Streptococcus* cell, and a *Streptomyces* cell.

27. An isolated polypeptide which is essential for the viability of a bacterial cell comprising the amino acid sequence as shown in any one of SEQ. ID NOS: 114-226.

28. An isolated polypeptide which is essential for the viability of a bacterial cell encoded by the isolated nucleic acid molecule of claim 1, 16, 17, or 18.

29. The isolated polypeptide of claim 27 or 28 which is a fusion polypeptide.

30. A method for producing a polypeptide having the amino acid sequence of any one of SEQ ID NOS: 114-226 or a polypeptide encoded by the polynucleotide sequence as shown in any one of Figures 26-130, comprising:

- a) culturing the host-vector system of claim 24 under suitable conditions so as to produce the polypeptide; and
- b) recovering the polypeptide so produced.

31. A polypeptide produced by the method of claim 30.

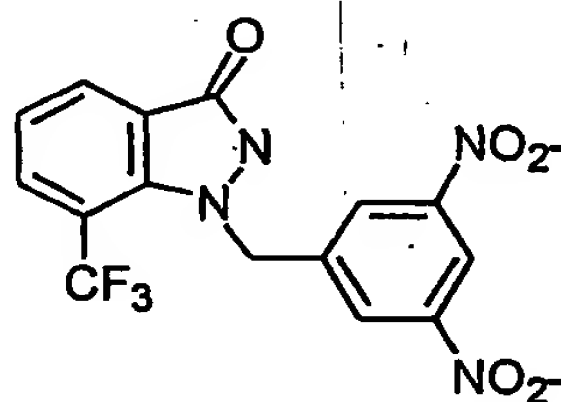
32. A ligand which binds the polypeptide of claim 27 or 28.

5 33. The ligand of claim 32 which is an antibody or an immunologically active fragment thereof.

34. The ligand of claim 33, wherein the antibody is a monoclonal antibody.

10 35. The ligand of claim 32 which is a diazalactone.

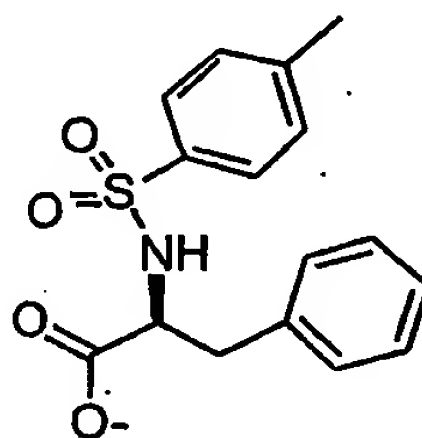
36. The ligand of claim 35, wherein the diazalactone comprises the structure:



37. The ligand of claim 32 which is a *N*-protected amino acid.

15

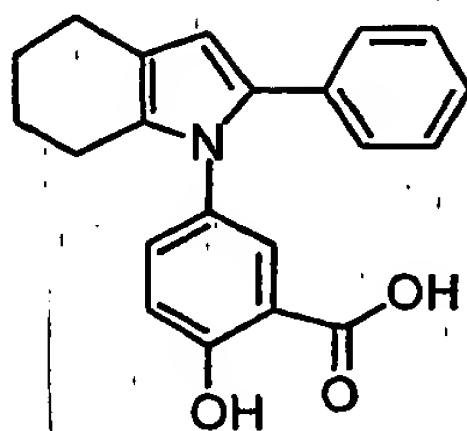
38. The ligand of claim 37, wherein the *N*-protected amino acid comprises the structure:



39. The ligand of claim 32 which is an azabicyclodiene.

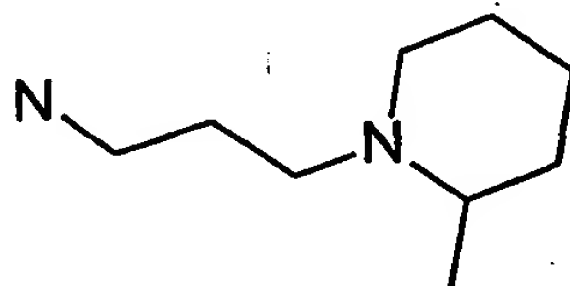
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40. The ligand of claim 39, wherein the azabicyclodiene comprises the structure:



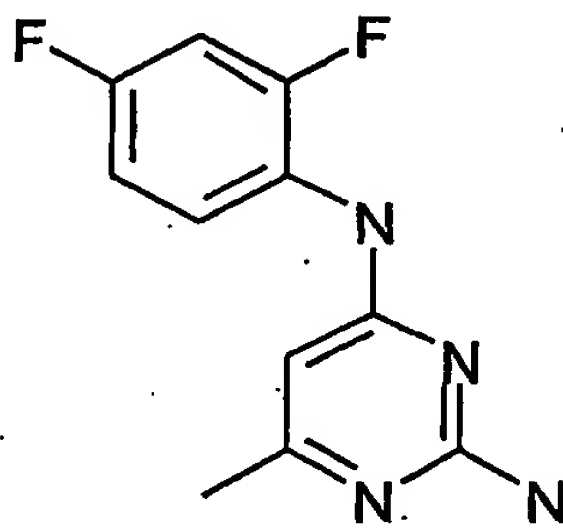
5 41. The ligand of claim 32 which is an alkaloid.

42. The ligand of claim 41, wherein the alkaloid comprises the structure:

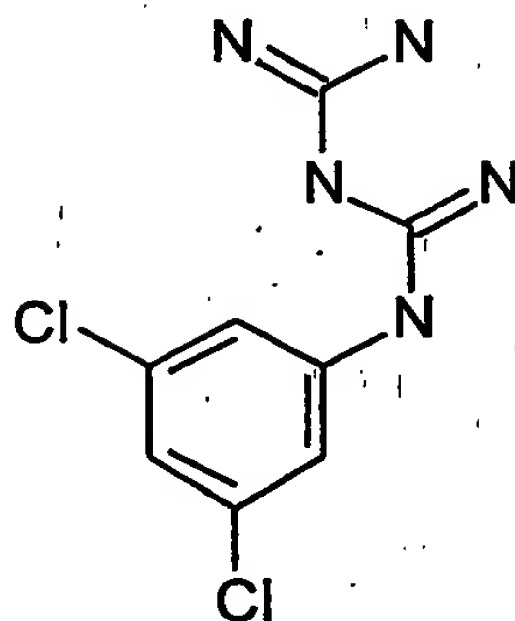


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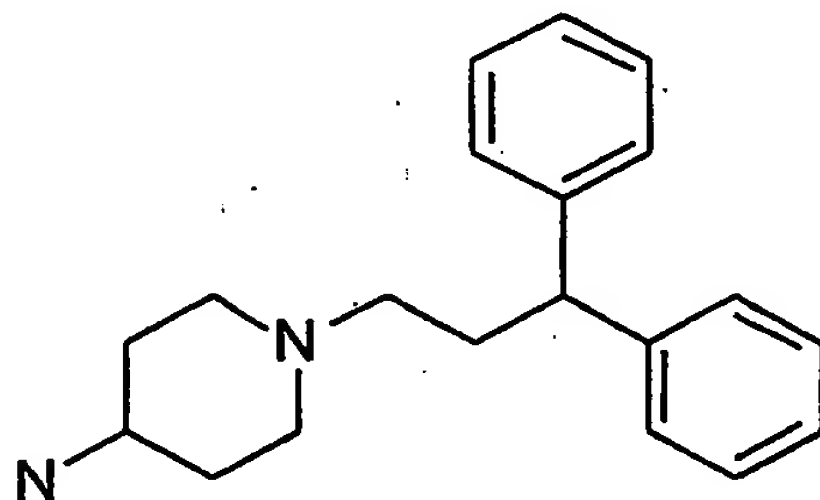
43. The ligand of claim 41, wherein the alkaloid comprises the structure:



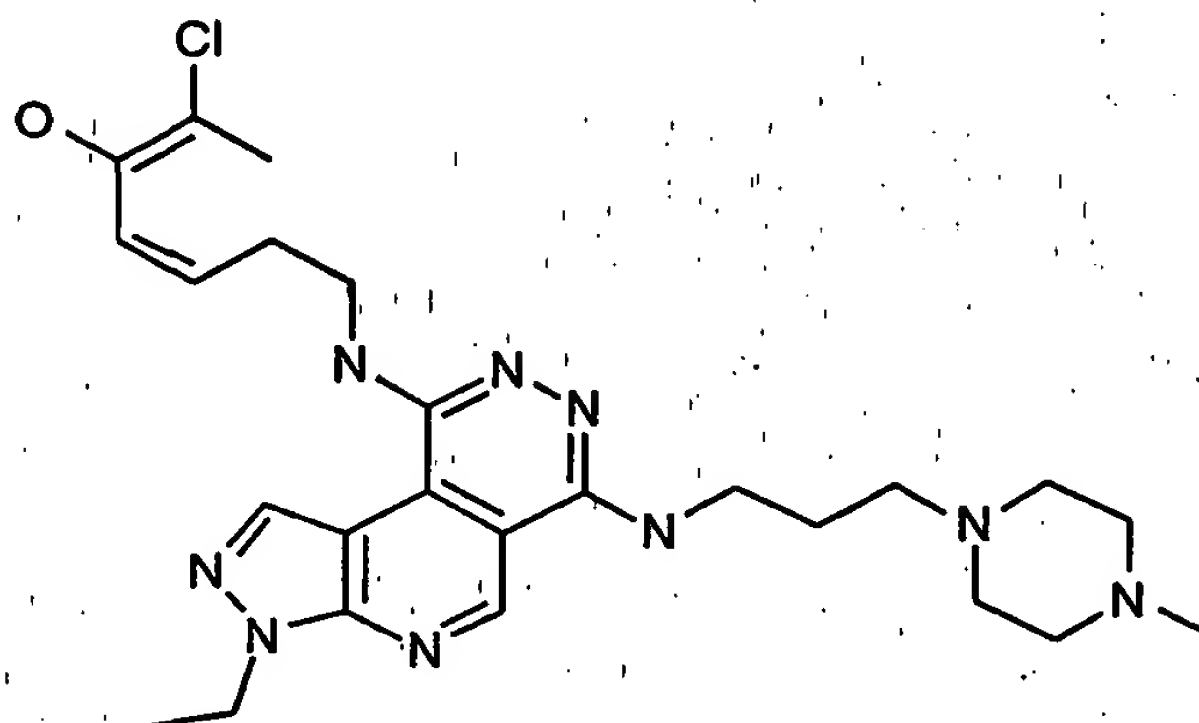
44. The ligand of claim 41, wherein the alkaloid comprises the structure:



5 45. The ligand of claim 41, wherein the alkaloid comprises the structure:



46. The ligand of claim 41, wherein the alkaloid comprises the structure:



5 47. A method for detecting the presence of the polypeptide of claim 27 or 28 in a sample, comprising contacting the sample with a ligand which binds the polypeptide and detecting the binding of the polypeptide with the ligand in the sample.

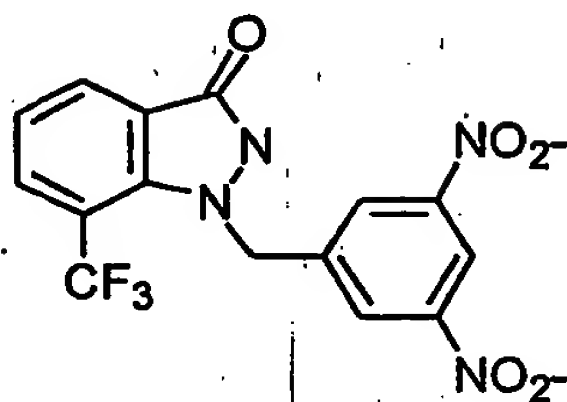
10 48. The method of claim 47, wherein the detecting comprises:
a) contacting the sample with the ligand; and
b) determining whether a polypeptide-ligand complex is so formed.

15 49. The method of claim 47, wherein the sample is a cell, a tissue, or a biological fluid.

50. The method of claim 47, wherein the sample is blood, serum, a swab from nose, a swab from ear, or a swab from throat.

20 51. The method of claim 47, wherein the ligand is a diazalactone.

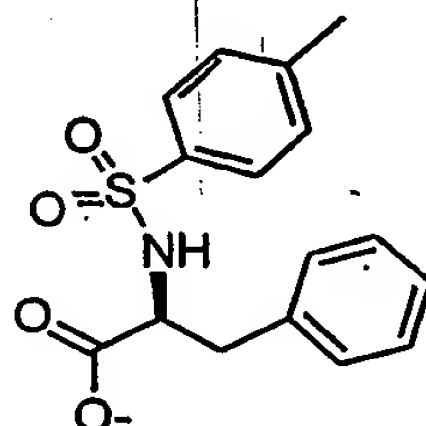
52. The method of claim 51, wherein the diazalactone comprises the structure:



53. The method of claim 47, wherein the ligand is a *N*-protected amino acid.

5

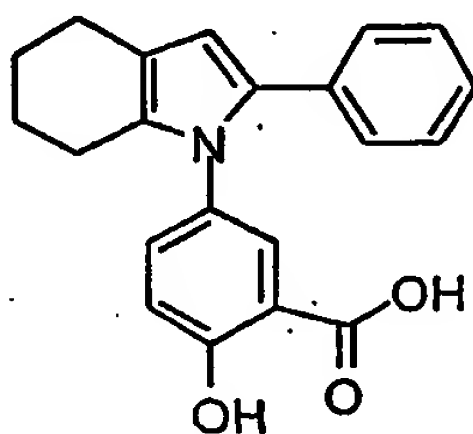
54. The method of claim 53, wherein the *N*-protected amino acid comprises the structure:



55. The method of claim 47, wherein the ligand is an azabicyclodiene.

10

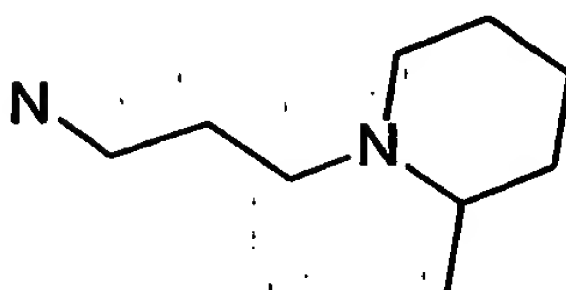
56. The method of claim 55, wherein the azabicyclodiene comprises the structure:



57. The ligand of claim 47 which is an alkaloid.

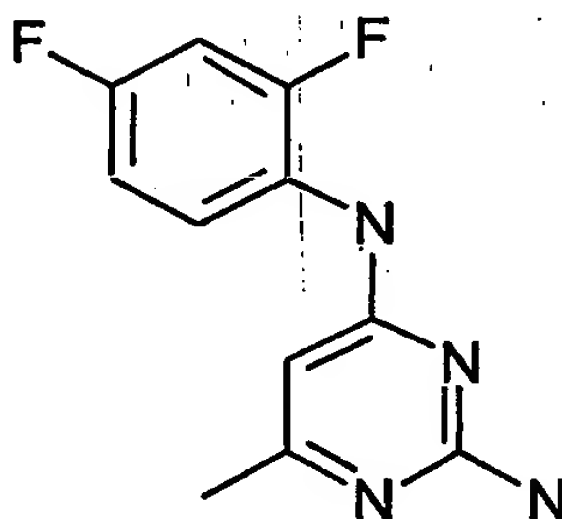
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58. The ligand of claim 57, wherein the alkaloid comprises the structure:

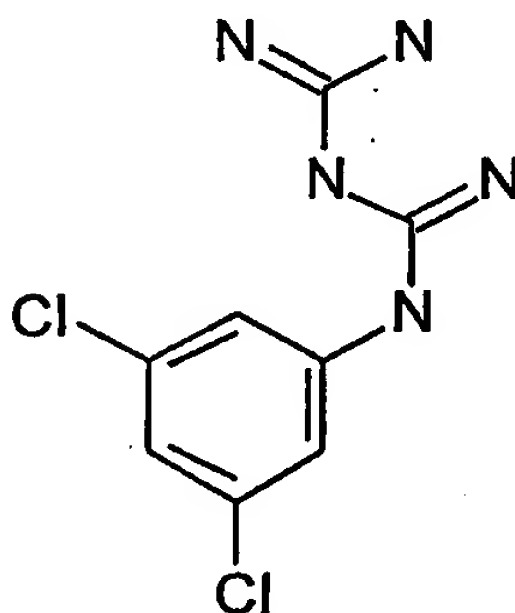


5

59. The ligand of claim 57, wherein the alkaloid comprises the structure:

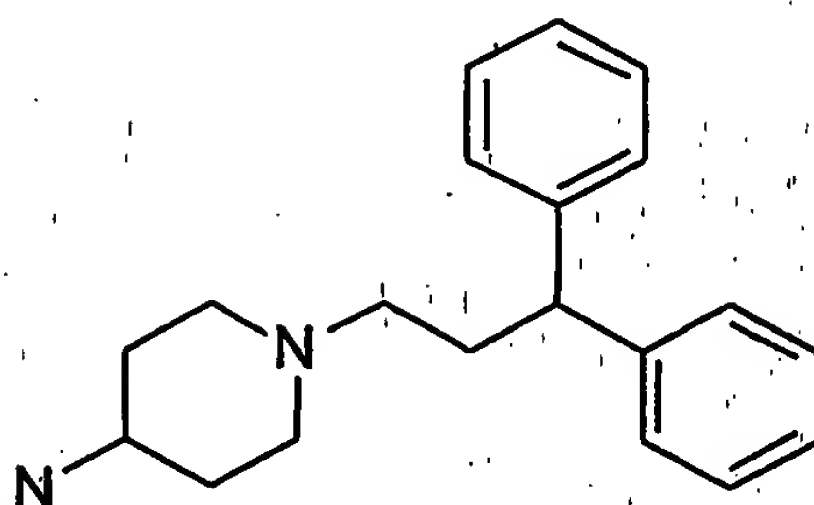


60. The ligand of claim 57, wherein the alkaloid comprises the structure:



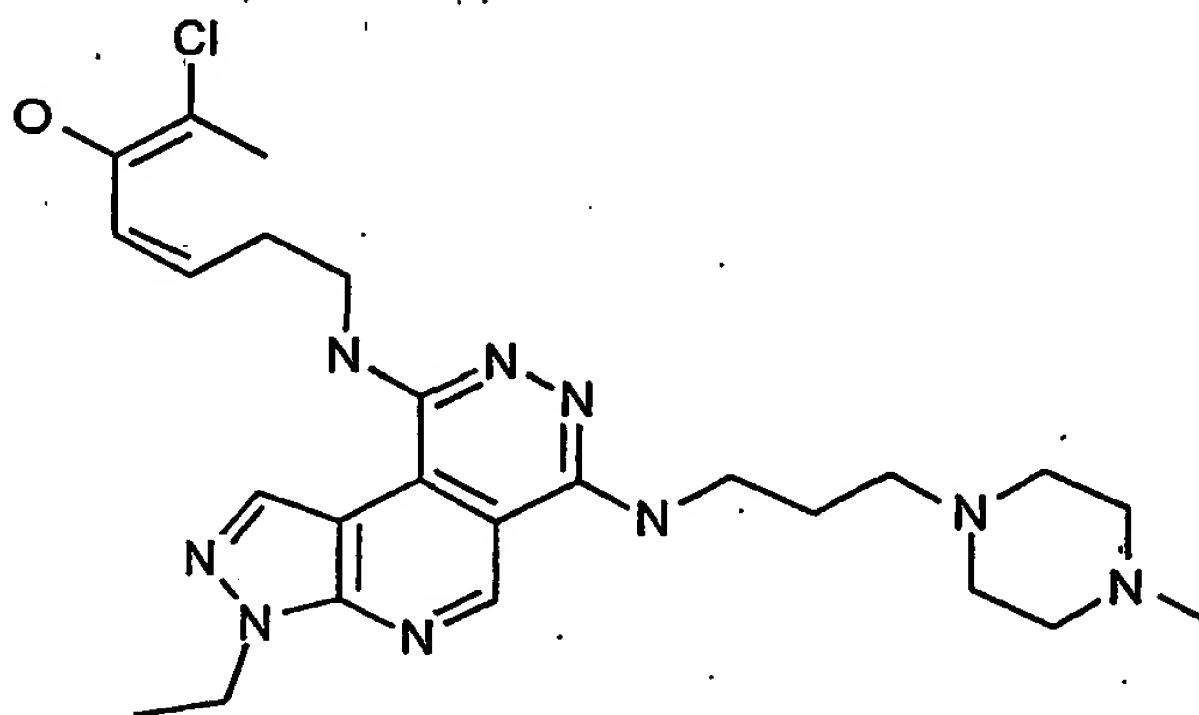
10

61. The ligand of claim 57, wherein the alkaloid comprises the structure:



5

62. The ligand of claim 57, wherein the alkaloid comprises the structure:



10

63. A method for detecting the presence of a target nucleic acid molecule as shown in any one of SEQ ID NOS:1-113 in a sample, comprising contacting the sample with the complementary nucleic acid molecule of claim 19 and detecting the binding of the target nucleic acid molecule with the complementary nucleic acid molecule in the sample.

15

64. The method of claim 63, wherein the detecting comprises:

- a) contacting the sample with the complementary nucleic acid molecule; and
- b) determining whether a complex comprising the target nucleic acid molecule and the complementary nucleic acid molecule is so formed.

65. The method of claim 63, wherein the sample is a cell, a tissue, or a biological fluid.

66. The method of claim 63, wherein the sample is blood, serum, a swab from nose, a swab from ear, or a swab from throat.

67. A pharmaceutical composition comprising the nucleic acid molecule of claim 1, 16, 17, or 18.

68. A pharmaceutical composition comprising the polypeptide of claim 27 or 28.

69. A pharmaceutical composition comprising the ligand of claim 32.

70. A method for determining whether a genomic nucleotide sequence of interest is essential for viability of a bacterial cell, comprising

- a. integrating an exogenous nucleotide sequence into the genomic nucleotide sequence of interest, wherein the exogenous nucleotide sequence comprises a portion of an open reading frame of the genomic nucleotide sequence of interest, and
- b. determining whether the cell having the genomic nucleotide sequence of interest so integrated is viable.

71. The method of claim 70, wherein the portion of the open reading frame comprises about 200 to 500 base pairs in length.

72. The method of claim 70, wherein the exogenous nucleotide sequence further comprises a nucleotide sequence conferring a selectable phenotype to the cell having the genome so integrated.

73. The method of claim 70, wherein determining comprises selecting the cell having the genome so integrated in the presence of a selection agent.

74. The method of claim 73, wherein the selection agent is chloramphenicol.

75. A nucleotide sequence of interest which is essential for viability of a bacterial cell isolated by the method of claim 70.

76. A bacterial cell comprising an exogenous nucleotide sequence integrated into the genomic nucleotide sequence of interest, generated by the method of claim 70.

77. A method for determining whether a genomic nucleotide sequence of interest resides within an operon, comprising

a) integrating an exogenous nucleotide sequence into the genomic nucleotide sequence of interest; and

b) determining whether the cell having the genomic nucleotide sequence of interest so integrated is viable, and wherein the exogenous nucleotide sequence lacks an expression regulatory sequence.

78. The method of claim 77, wherein the exogenous nucleotide sequence further comprises a nucleotide sequence conferring a selectable phenotype to the cell having the genome so integrated.

79. The method of claim 77, wherein determining comprises selecting the cell having the genome so integrated in the presence of a selection agent.

80. The method of claim 79, wherein the selection agent is chloramphenicol.

5 81. A method for inhibiting a function of a CEG polypeptide which is essential for viability of a bacterial cell, the method comprising contacting the CEG polypeptide with the ligand of claim 32 under suitable conditions thereby inhibiting the function of the CEG polypeptide.

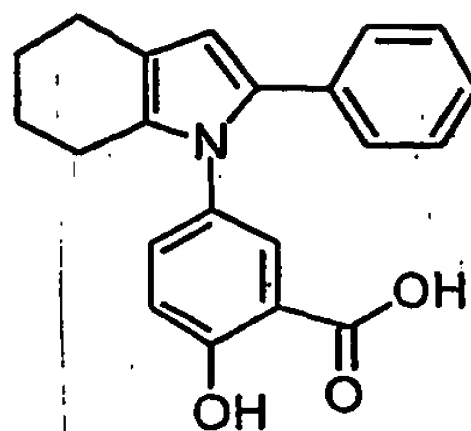
10 82. The method of claim 81, wherein the function of the CEG polypeptide is selected from a group consisting of a pantothenate kinase, a Holliday Junction branch migration protein, a single stranded DNA binding protein, a phosphoglucosamine mutase, an acetyltransferase, an uridylyltransferase, a malonyl CoenzymeA:ACP transacylase, a 3-oxoacyl-ACP synthase II, a 3-oxoacyl-ACP reductase, a phosphomethylpyrimidine (HMP-P) kinase, a GTP binding protein, a ATP
15 binding protein, or a 4-aminoimidazole carboxylase.

83. The method of claim 81, wherein the CEG polypeptide is selected from a group consisting of CFE1-113.

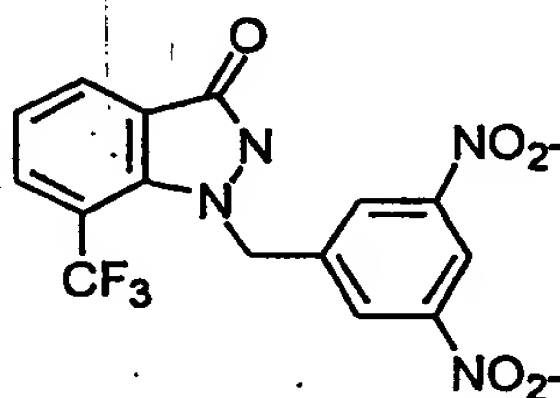
20 84. The method of claim 81, wherein the CEG polypeptide is 2CFE 34 shown in Figure 55.

85. The method of claim 81, wherein the CEG polypeptide is 2CFE 43 shown in
25 Figure 64.

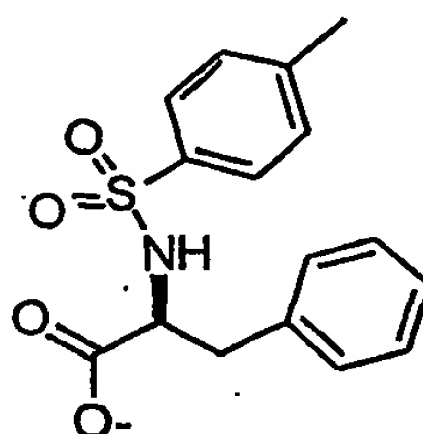
86. The method of claim 81, wherein the CEG polypeptide is 2CFE 34 shown in Figure 55 and the ligand is:



5 87. The method of claim 81, wherein the CEG polypeptide is 2CFE 43 shown in Figure 64 and the ligand is:



10 88. The method of claim 81, wherein the CEG polypeptide is 2CFE 43 shown in Figure 64 and the ligand is:



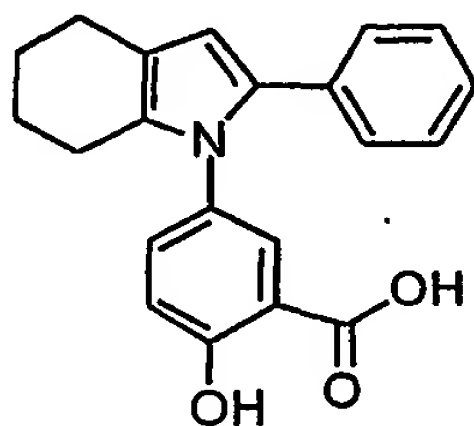
89. A method for identifying a ligand in a sample which specifically binds a CEG polypeptide, the method comprising:

- a) contacting the CEG polypeptide with the sample under suitable conditions so that a complex having the CEG polypeptide and the ligand is formed;
- b) recovering the complex so formed ; and
- c) separating the CEG polypeptide from the ligand in the complex and identifying the ligand so separated.

90. The method of claim 89, wherein the sample is a tissue or biological fluid.

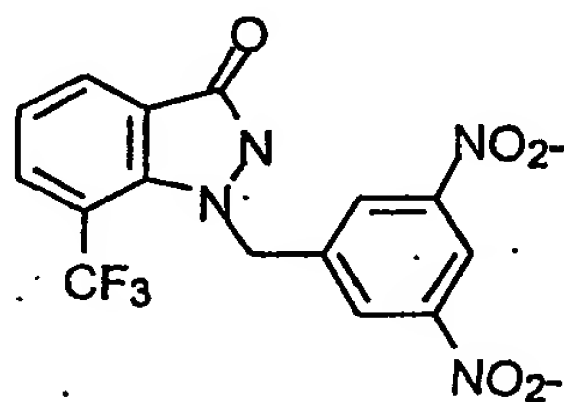
91. The method of claim 89, wherein the ligand is an azabicyclodiene.

92. The method of claim 91, wherein the azabicyclodiene comprises the structure:



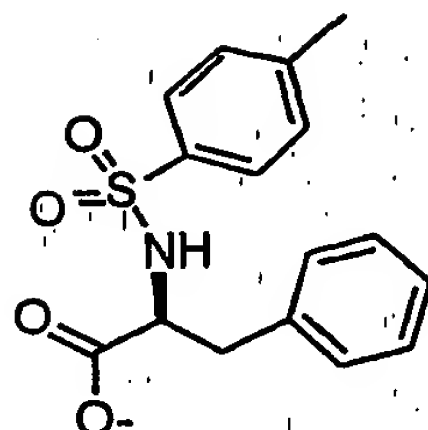
93. The method of claim 89, wherein the ligand is a diazalactone.

94. The method of claim 93, wherein the diazalactone comprises the structure:



95. The method of claim 89, wherein the ligand is a *N*-protected amino acid.

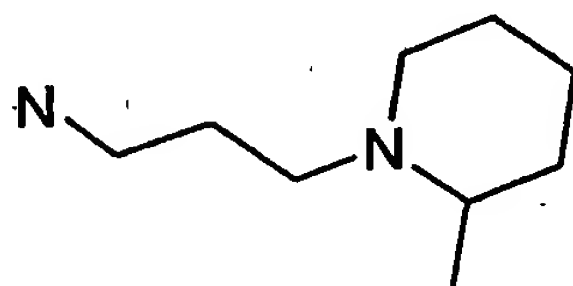
96. The method of claim 95, wherein the *N*-protected amino acid comprises the structure:



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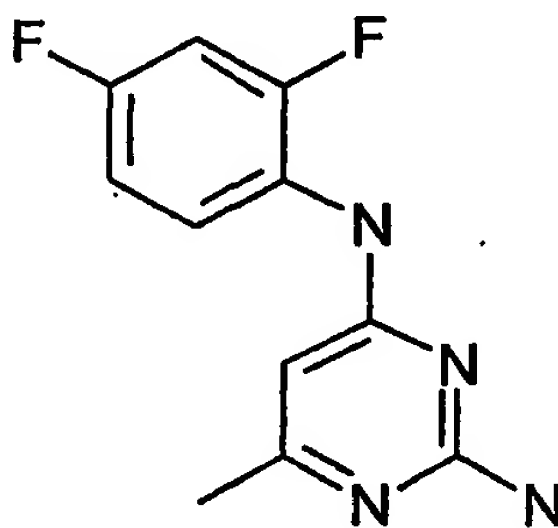
97. The method of claim 89, wherein the ligand is an alkaloid.

98. The ligand of claim 97, wherein the alkaloid comprises the structure:



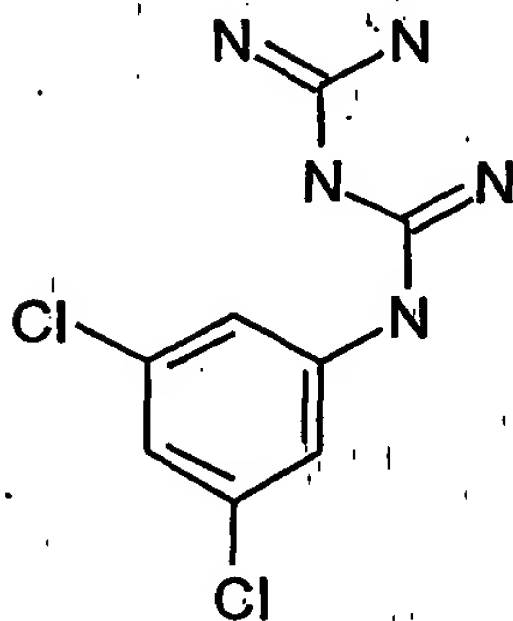
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99. The ligand of claim 97, wherein the alkaloid comprises the structure:

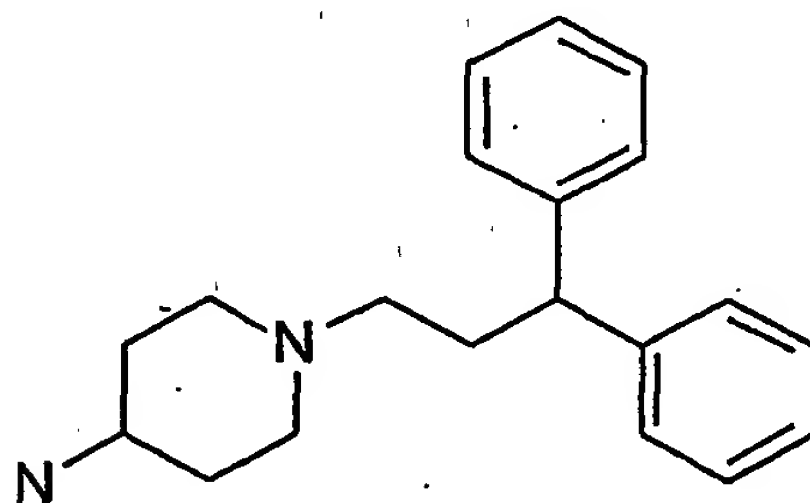


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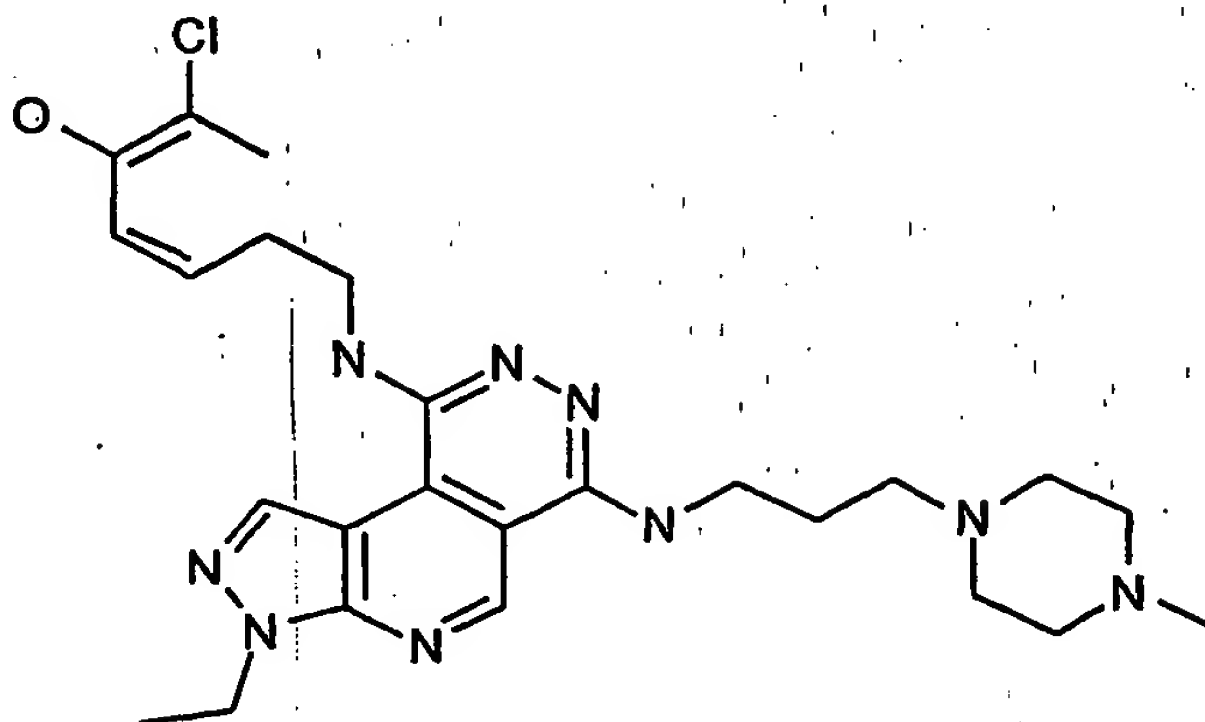
100. The ligand of claim 97, wherein the alkaloid comprises the structure:



101. The ligand of claim 97, wherein the alkaloid comprises the structure:



102. The ligand of claim 97, wherein the alkaloid comprises the structure:



Gene Disruption Assay

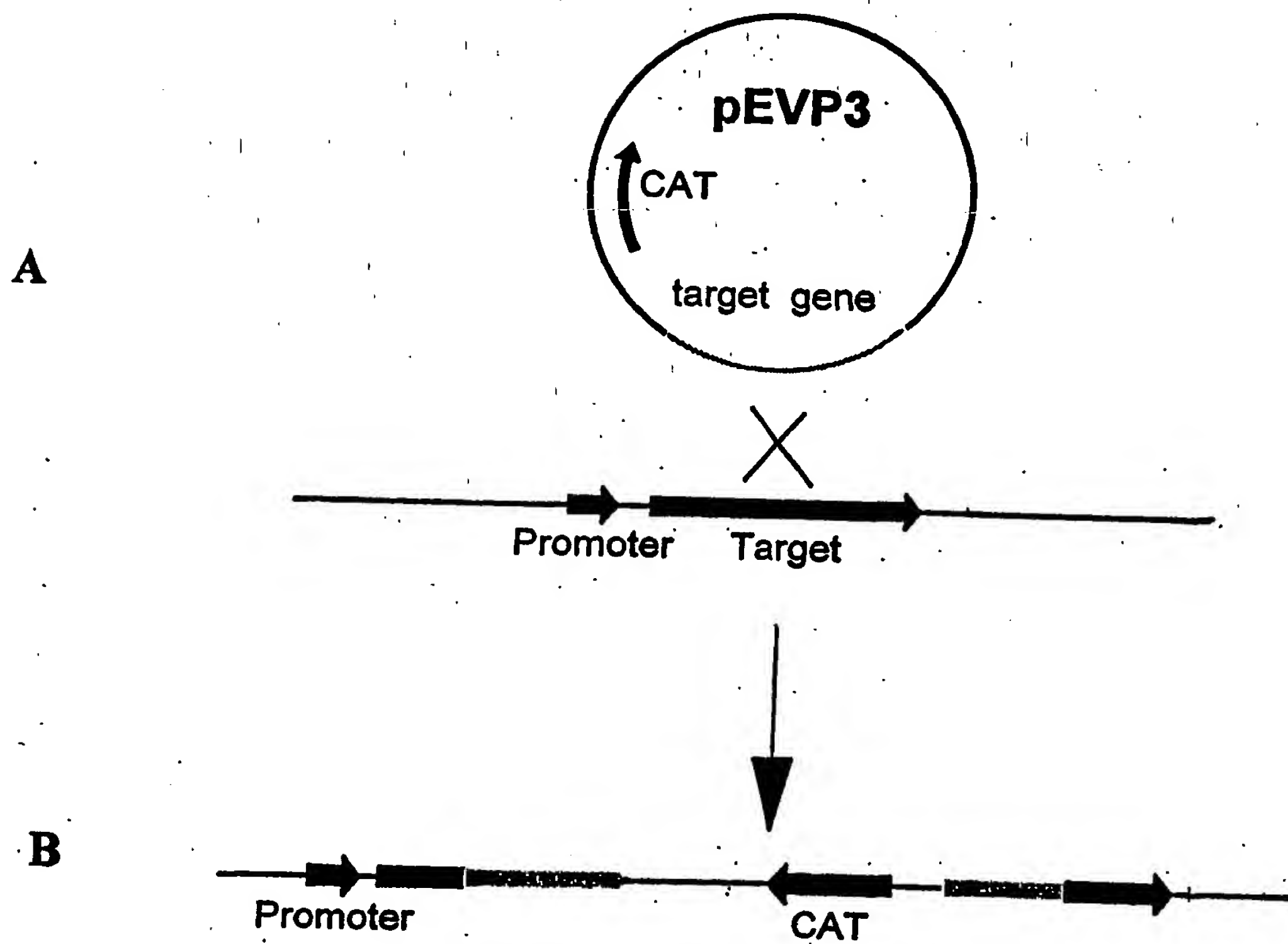


FIGURE 1

Polarity test for Operons

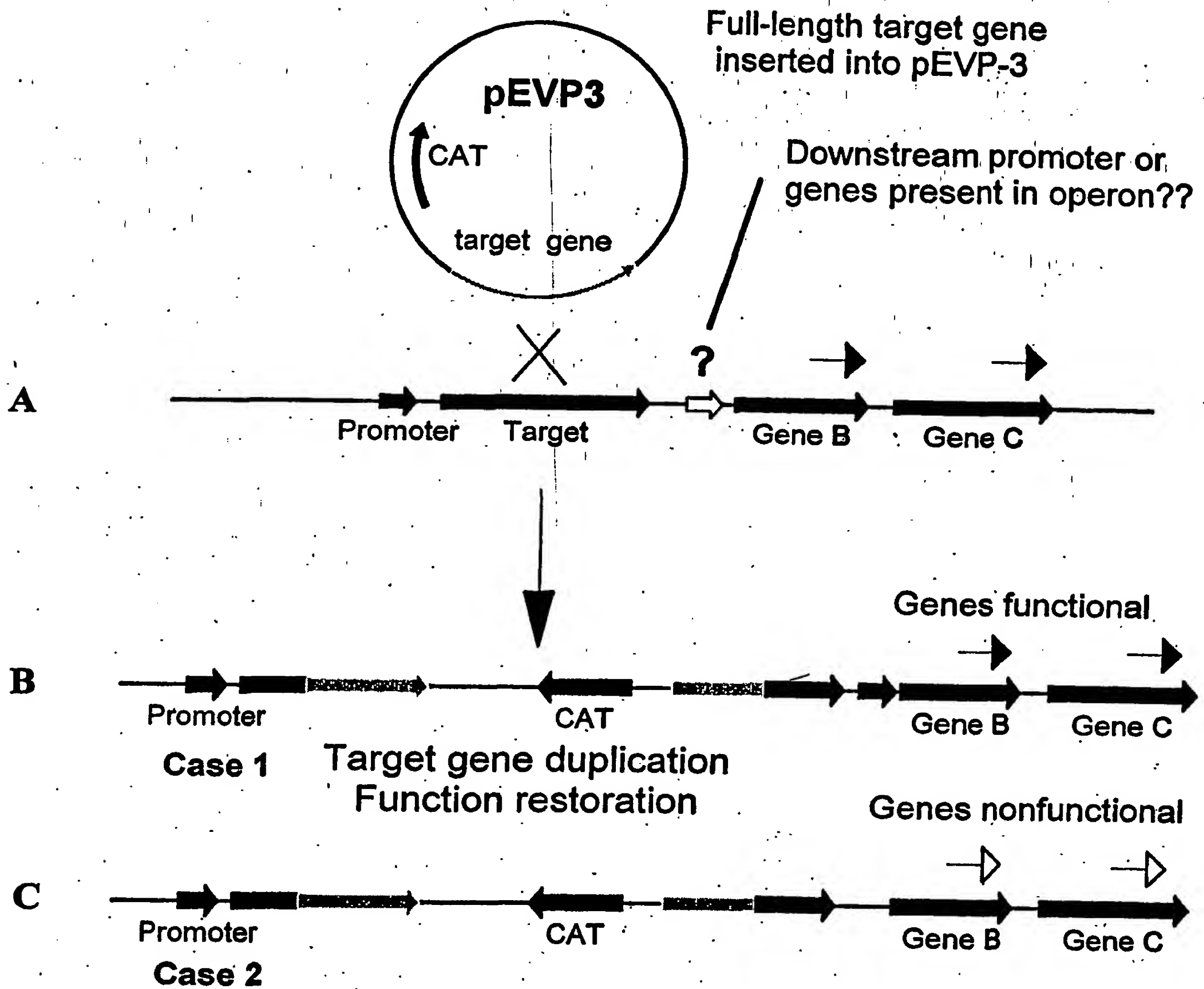
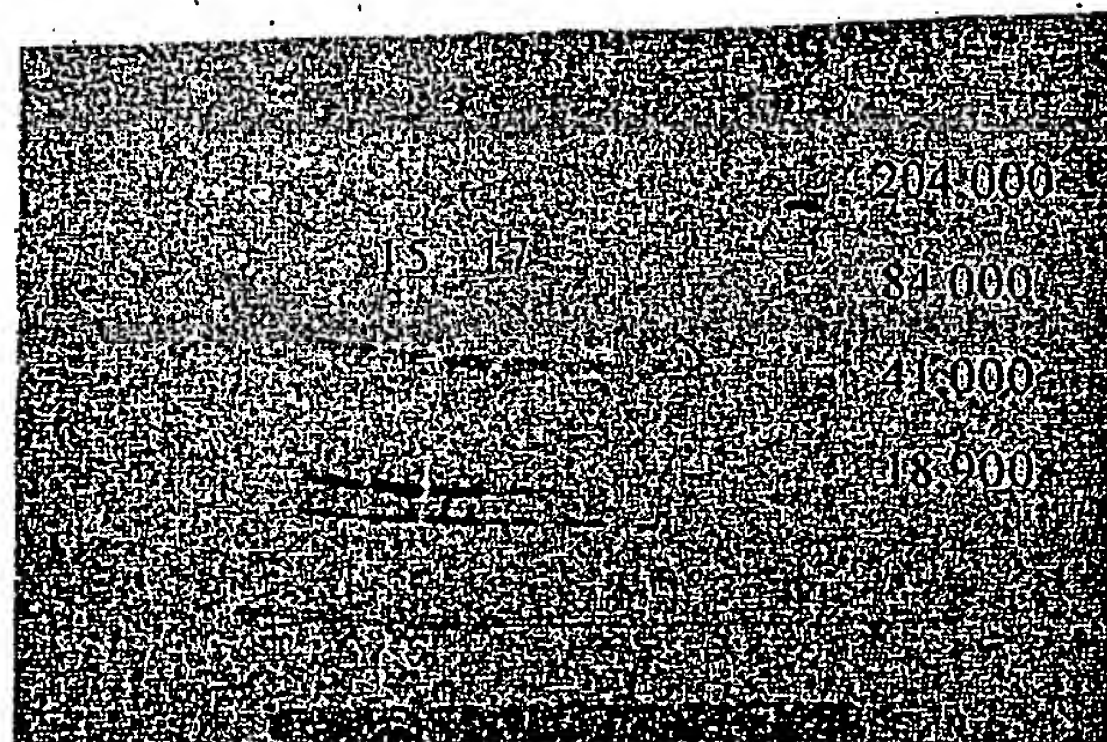


FIGURE 2

A.



B.

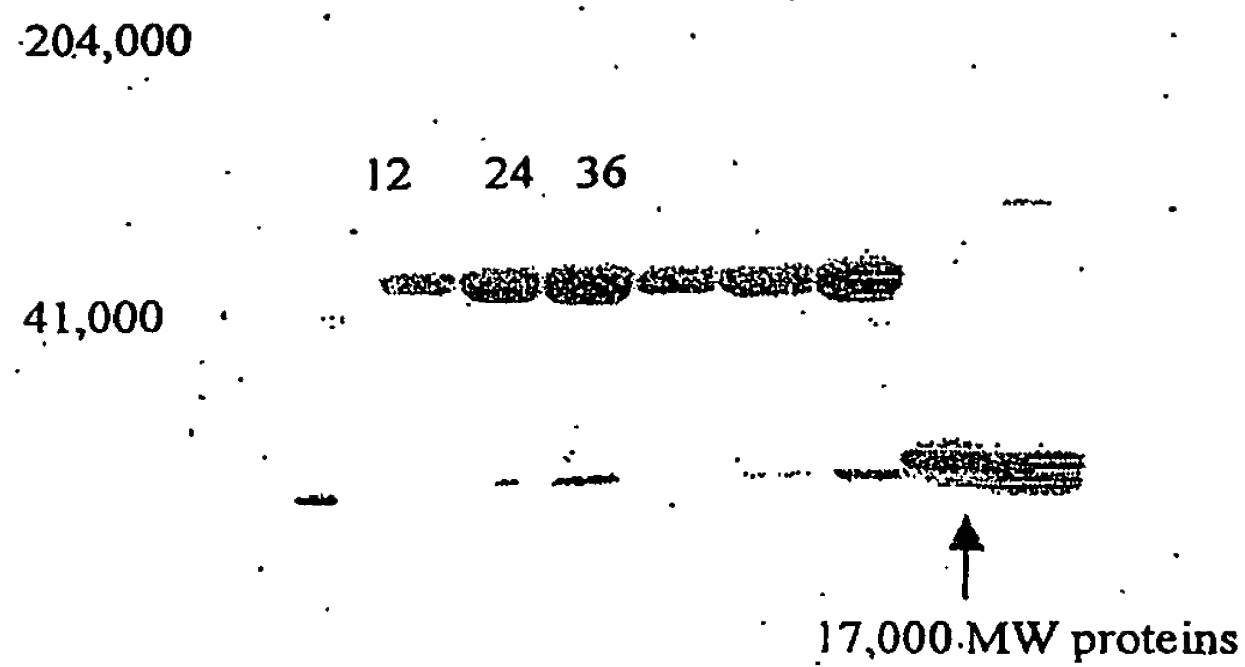


FIGURE 3

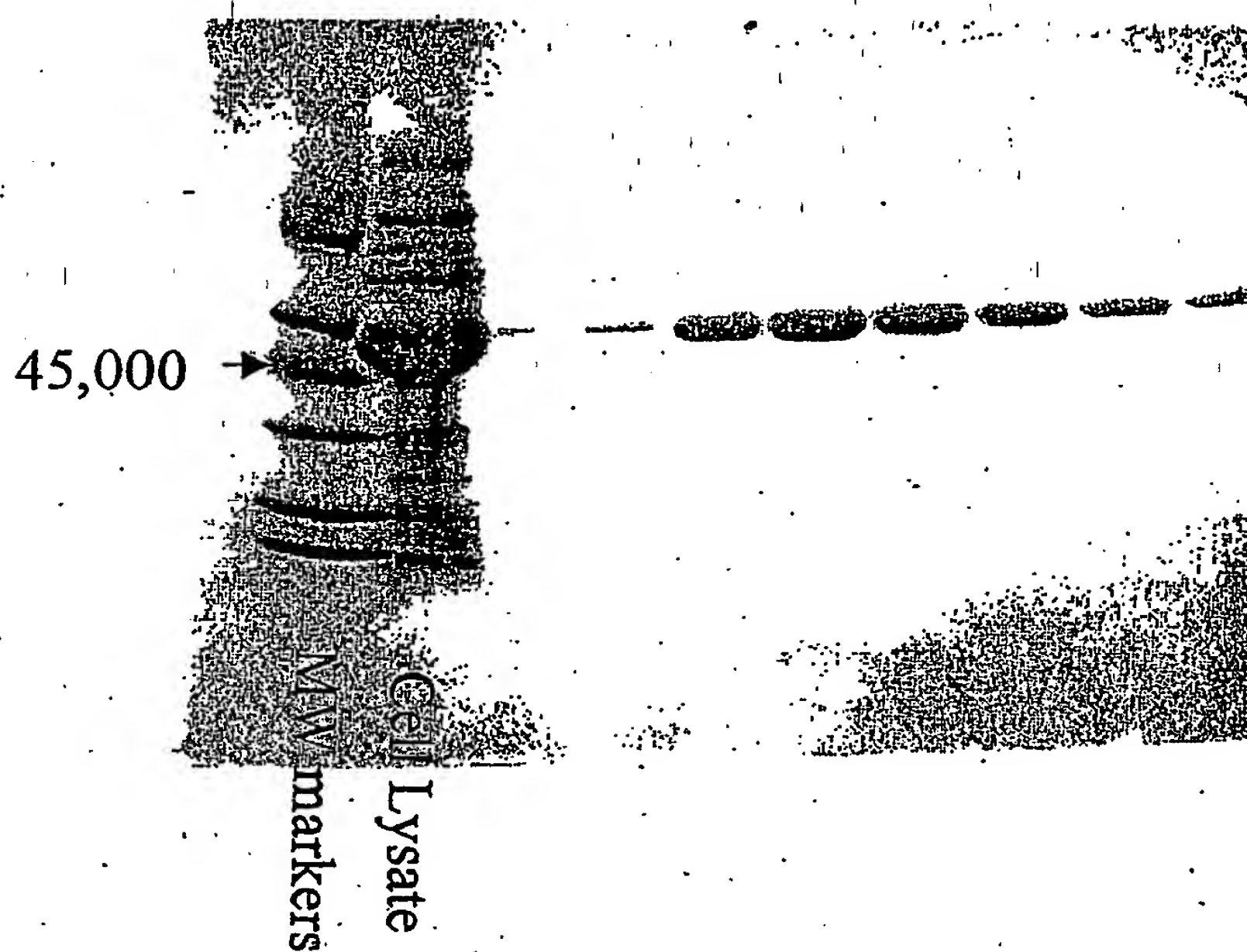


FIGURE 4

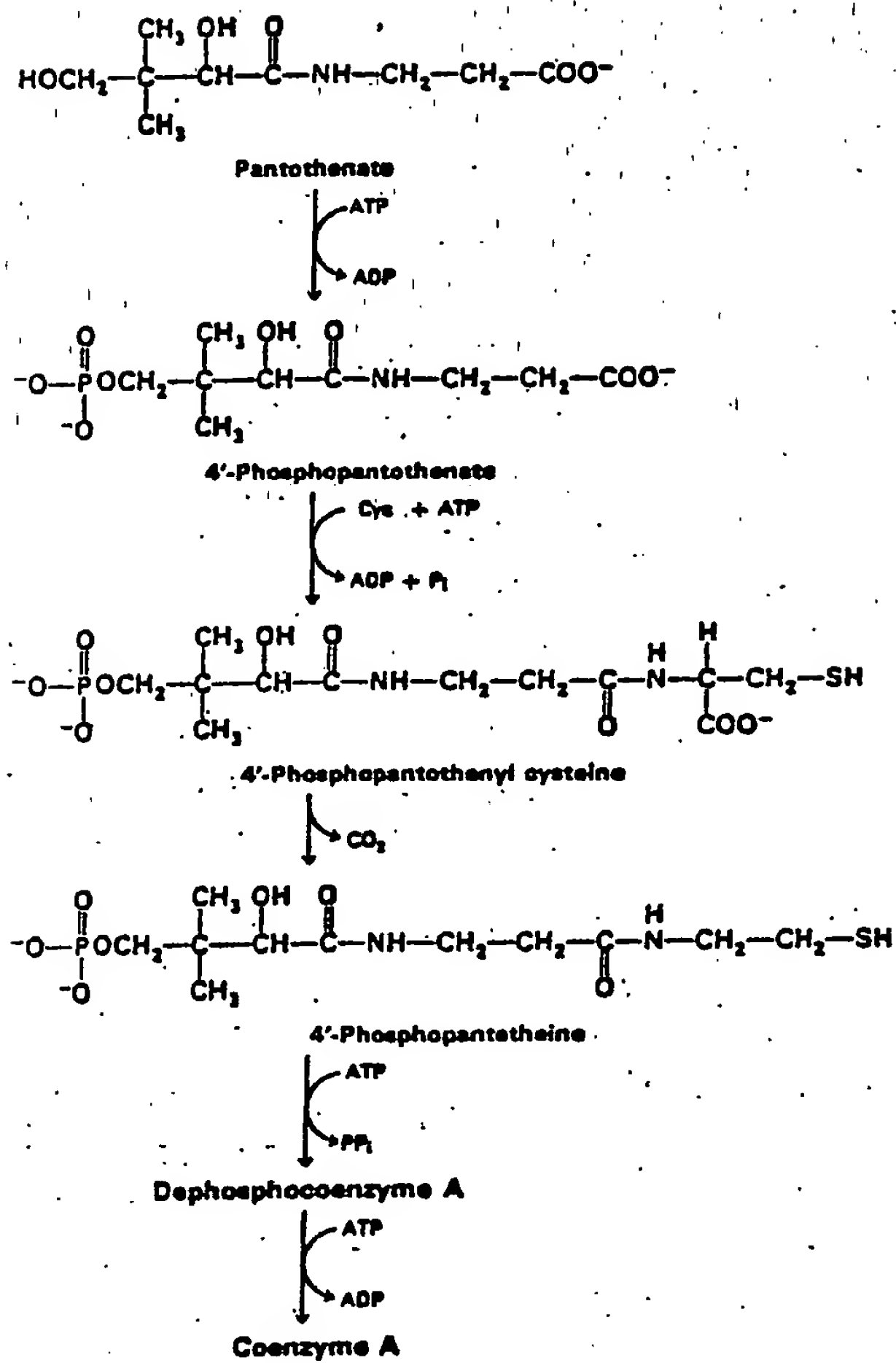
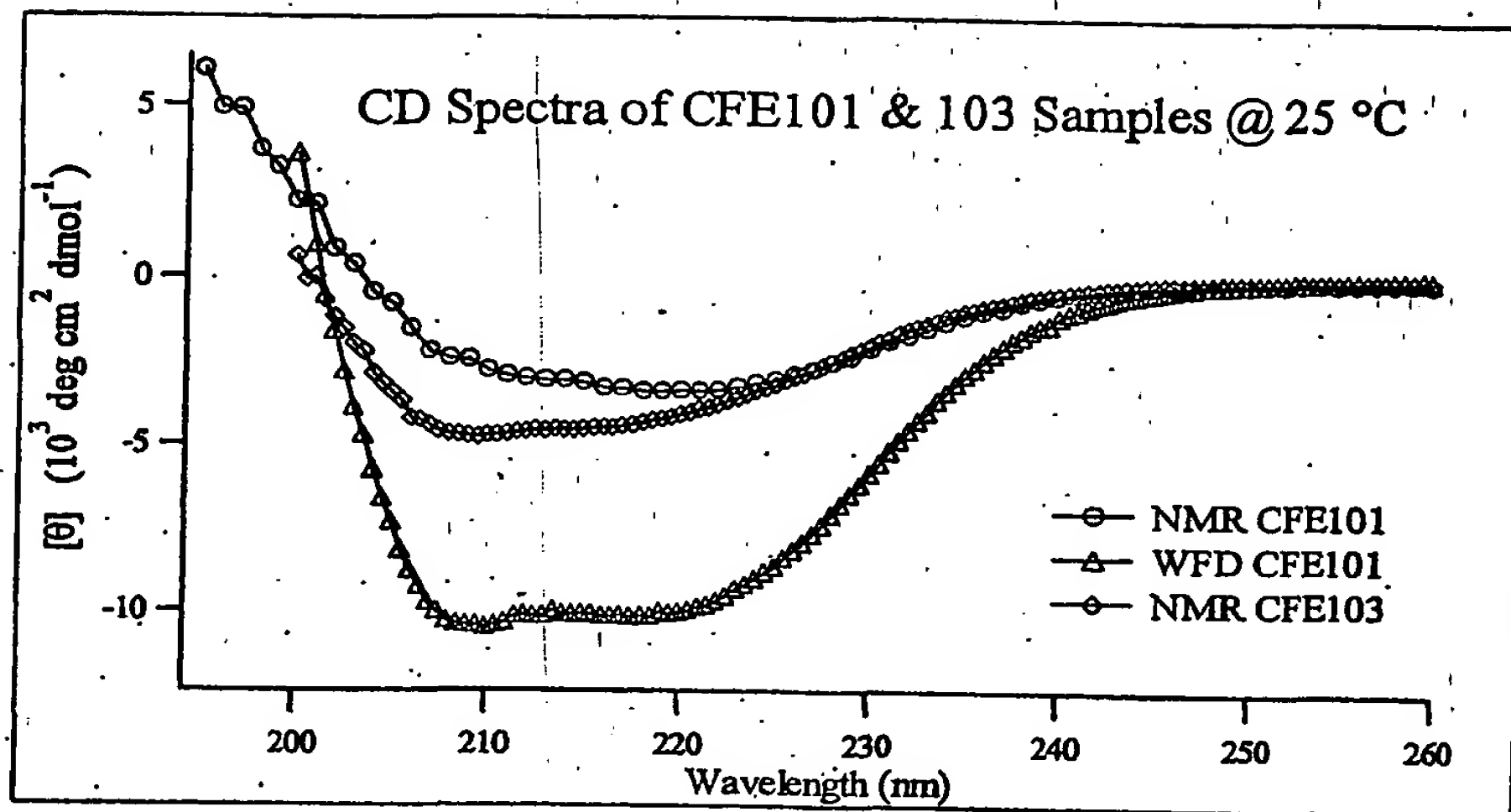


FIGURE 5

A.



B.

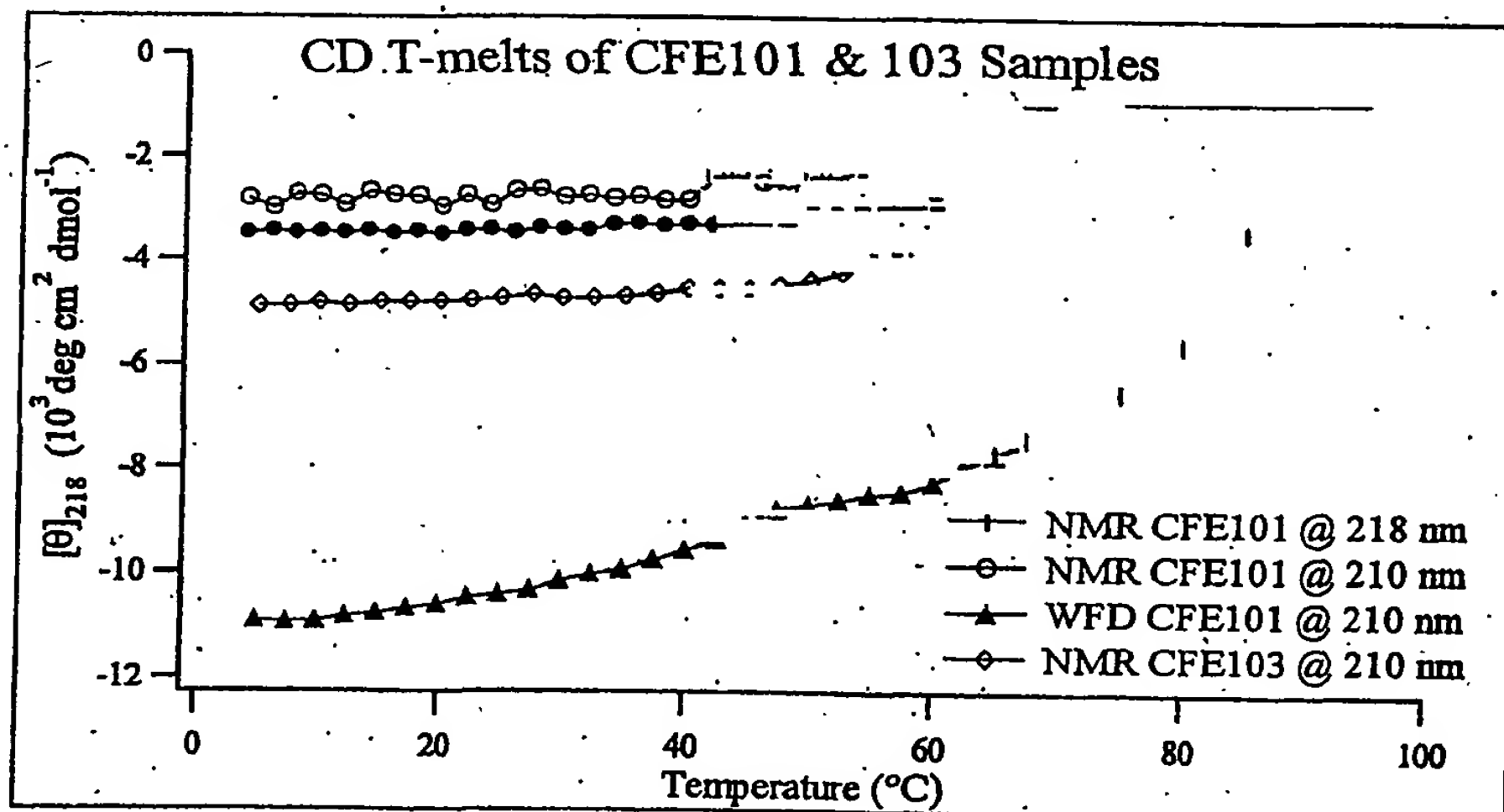
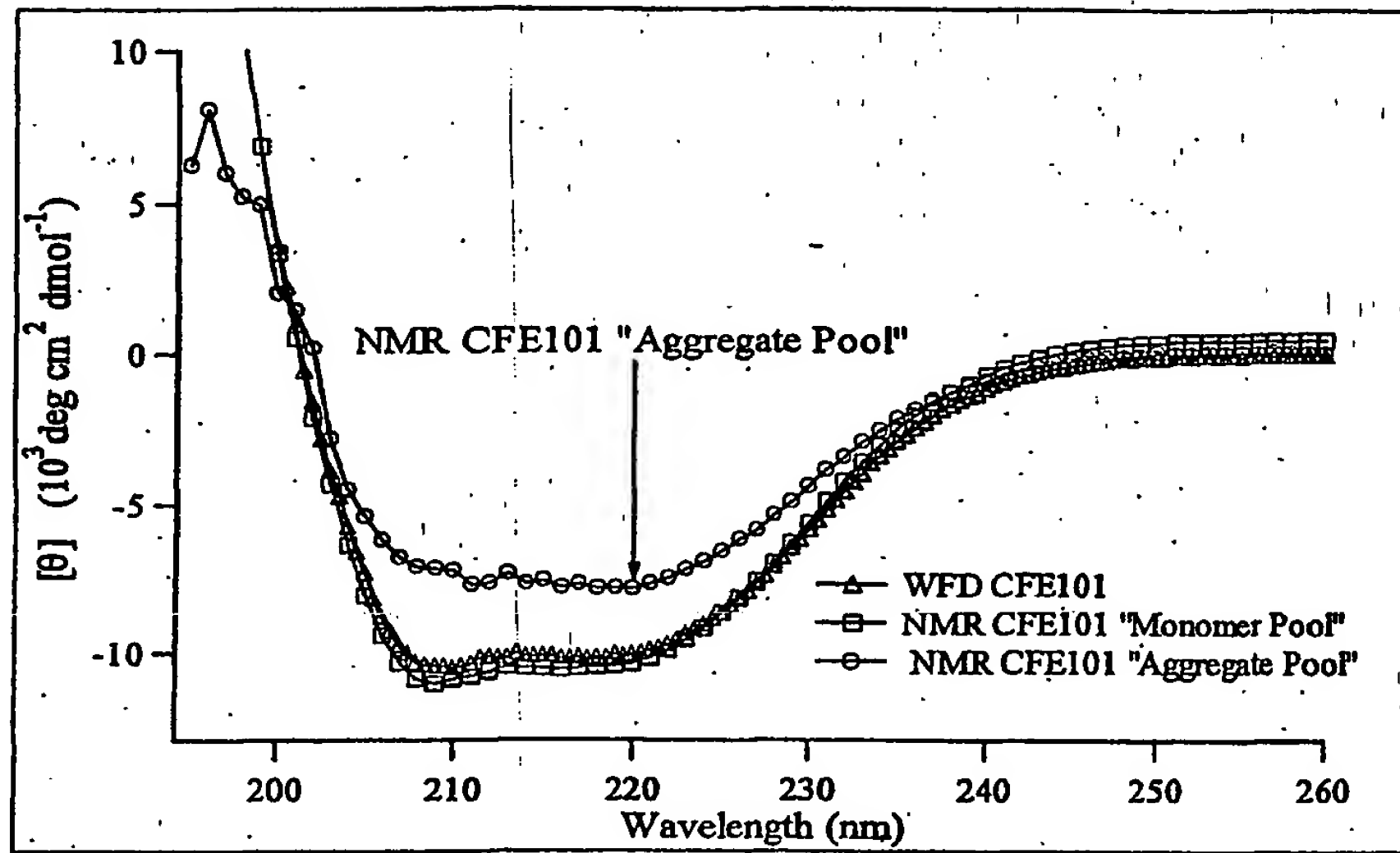


FIGURE 6

A.



B.

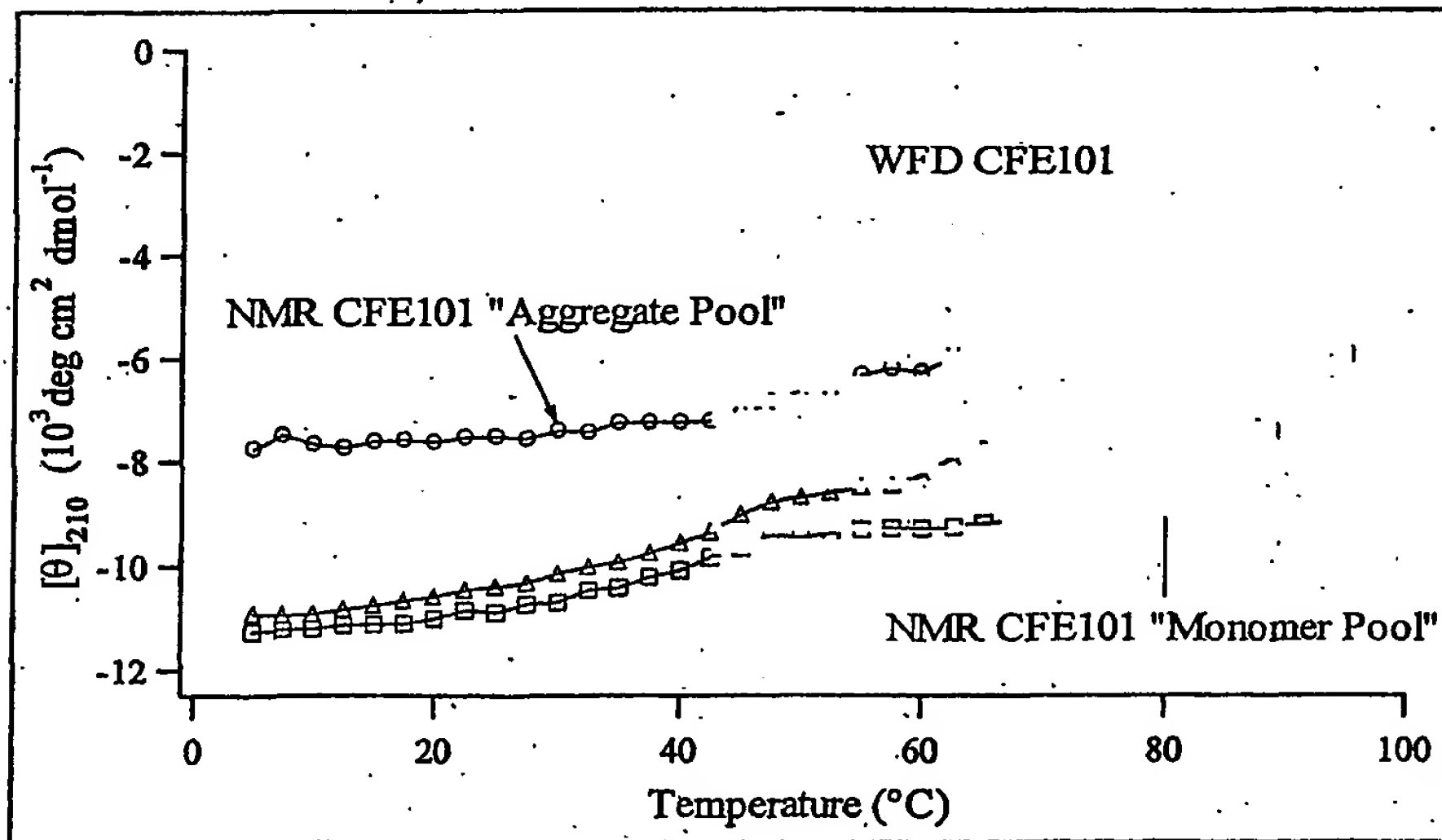


FIGURE 7

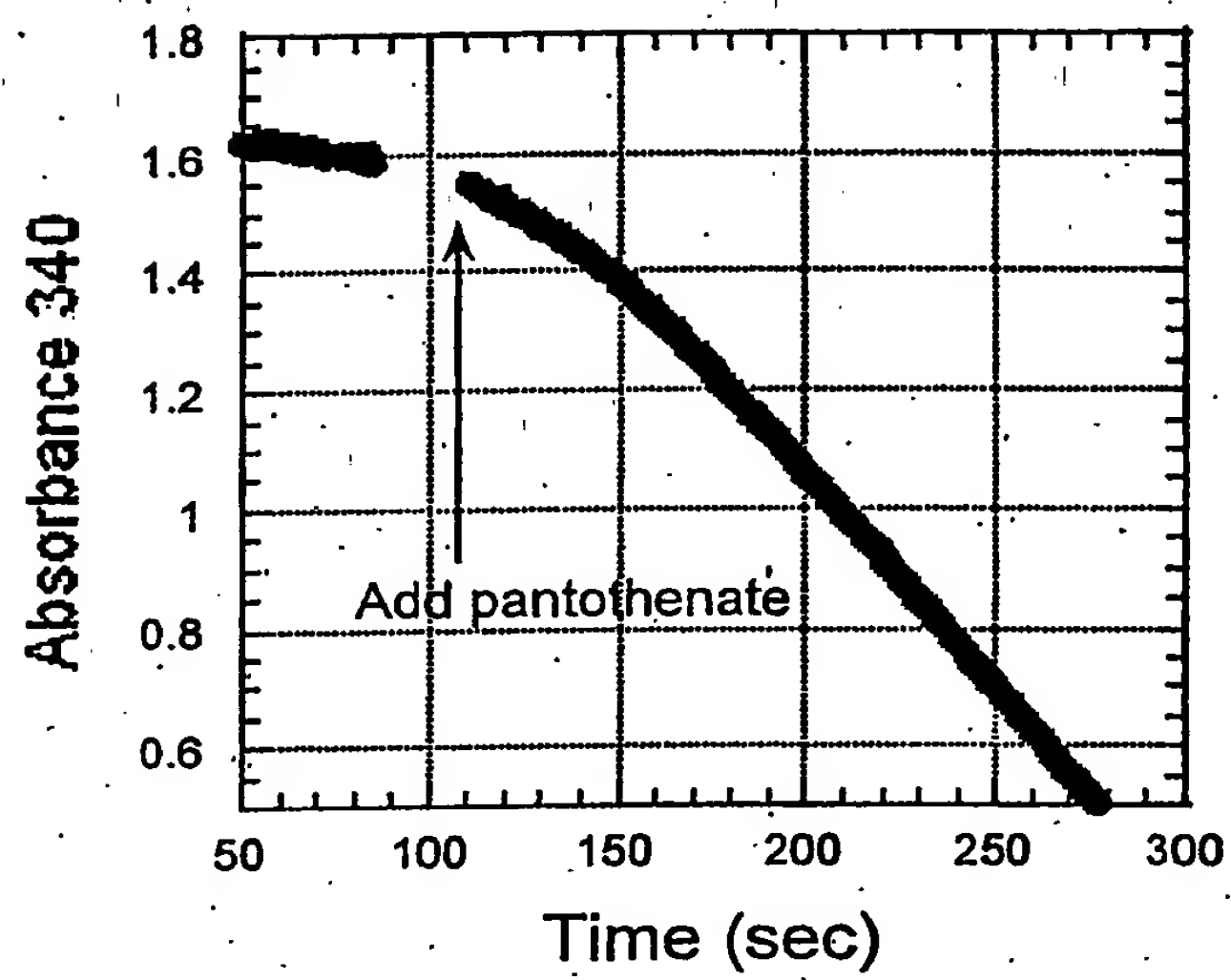


FIGURE 8

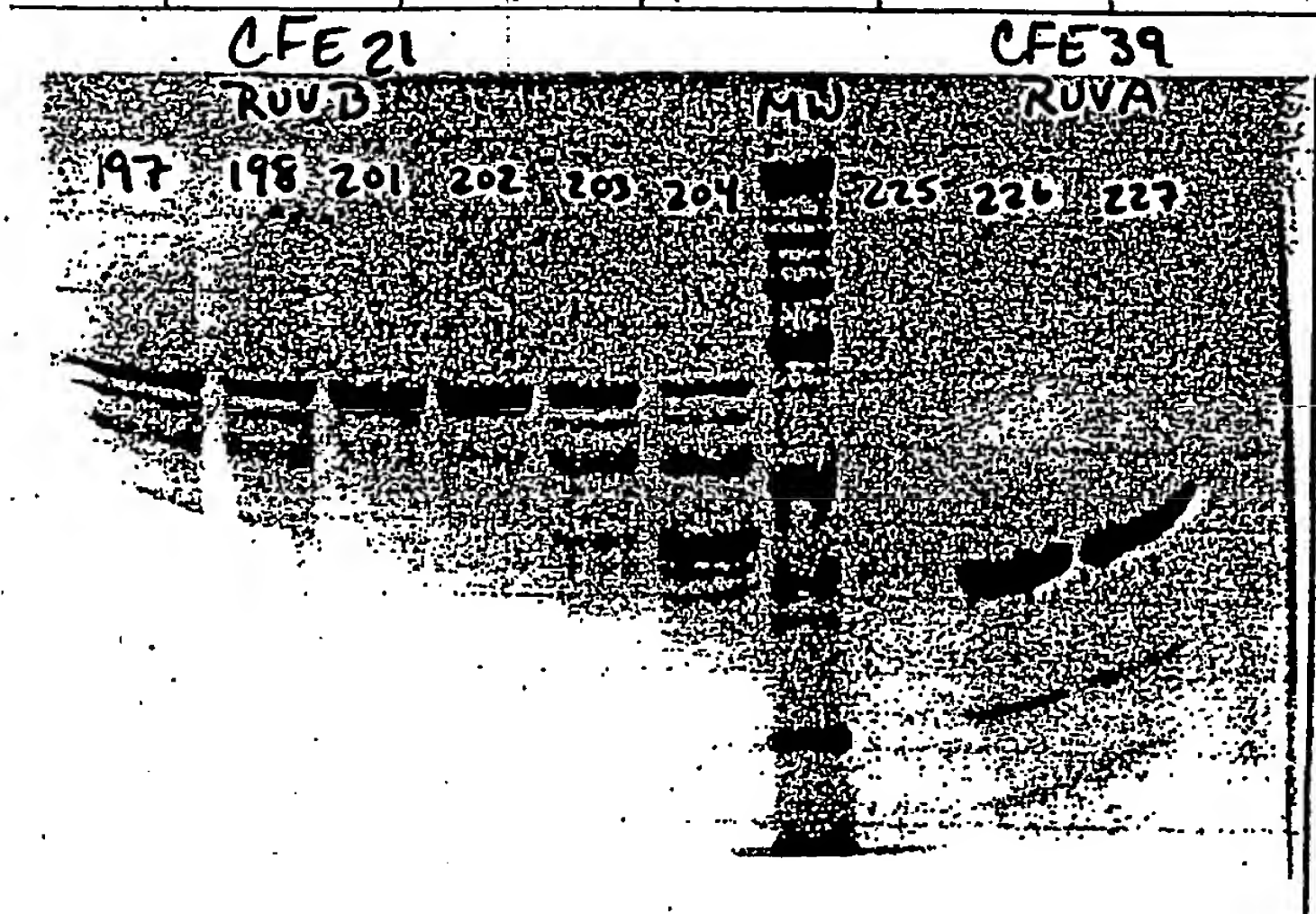


FIGURE 9

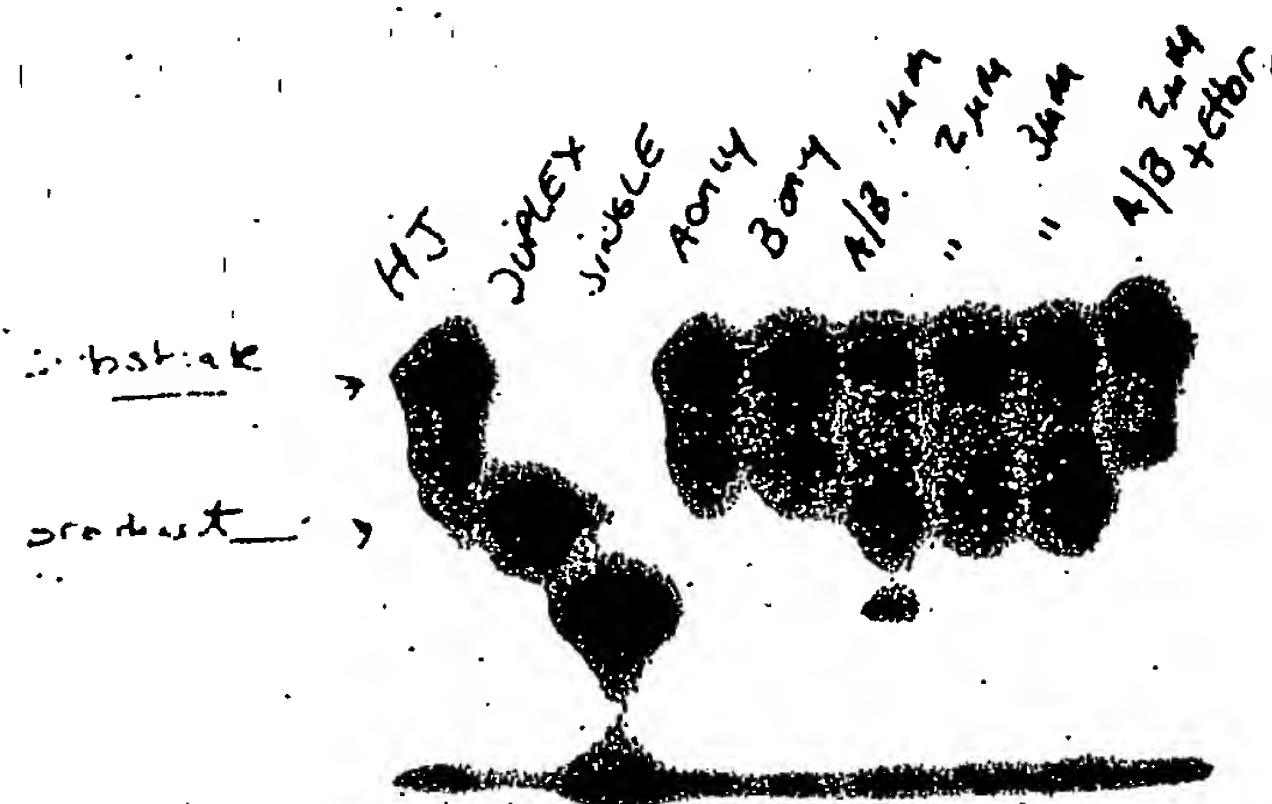


FIGURE 10

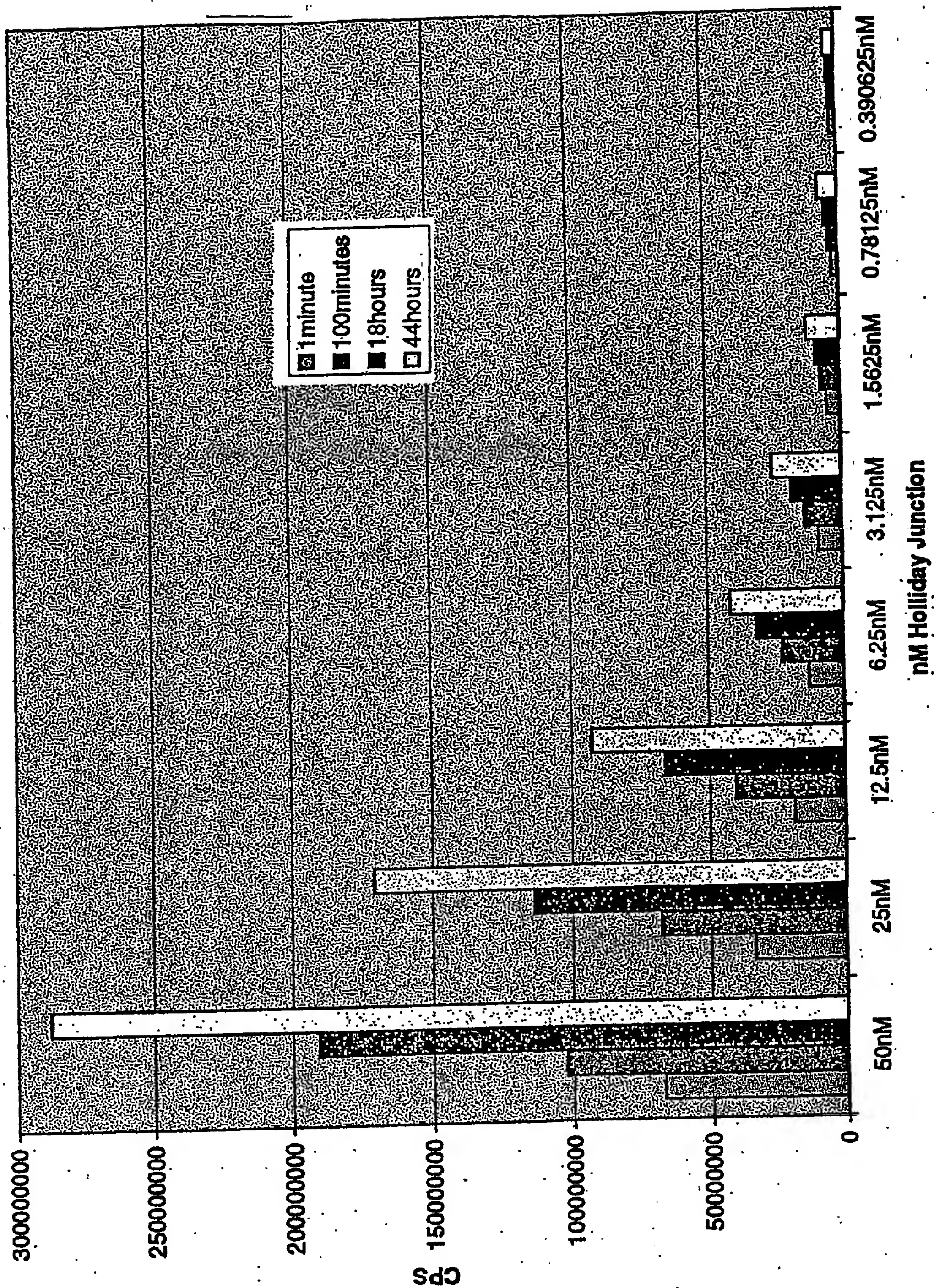


FIGURE 11

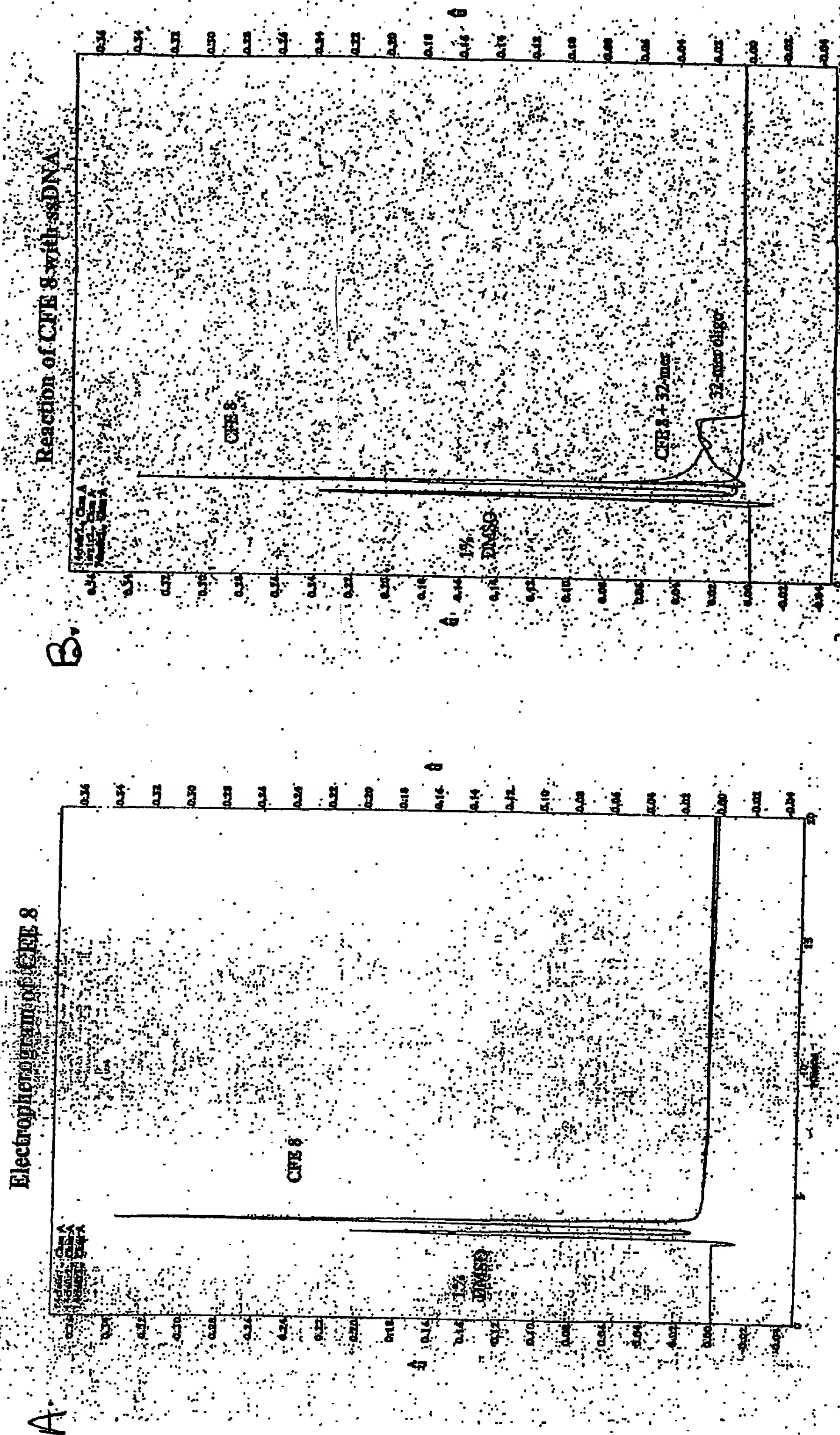
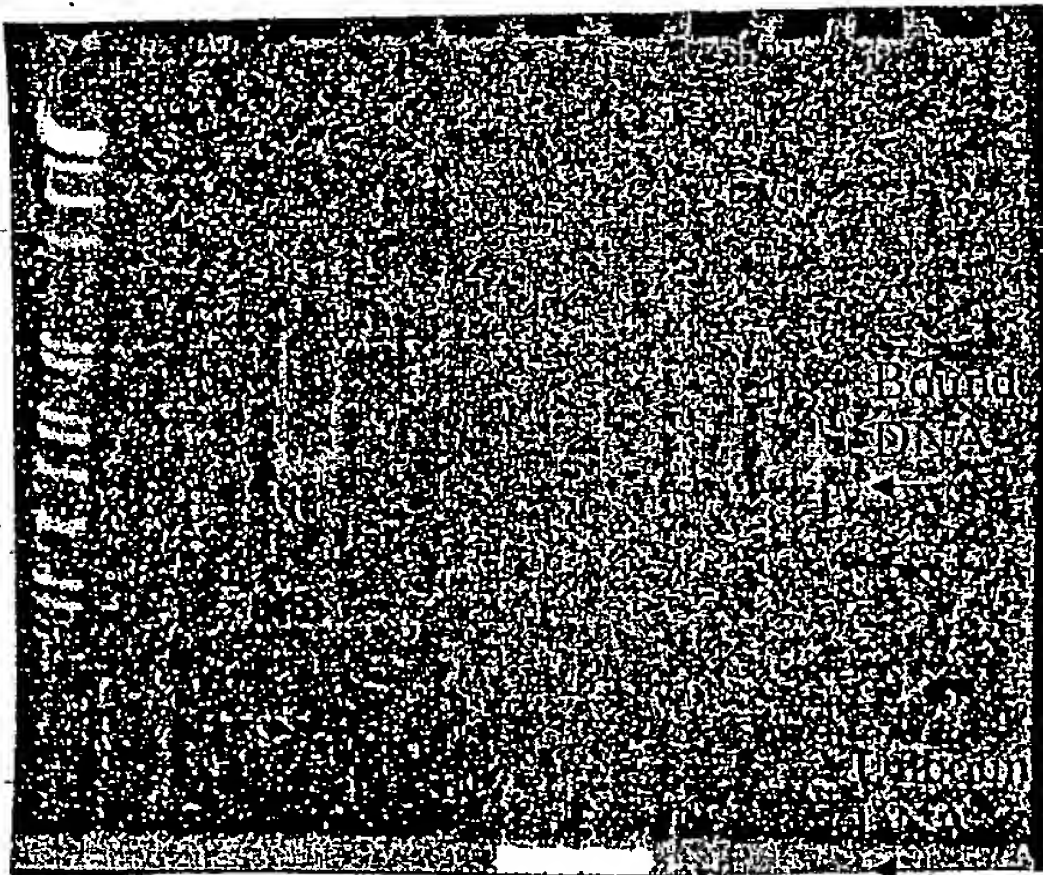


FIGURE 12

A.

Minus BSA

Plus BSA



B.

Minus BSA

Plus BSA

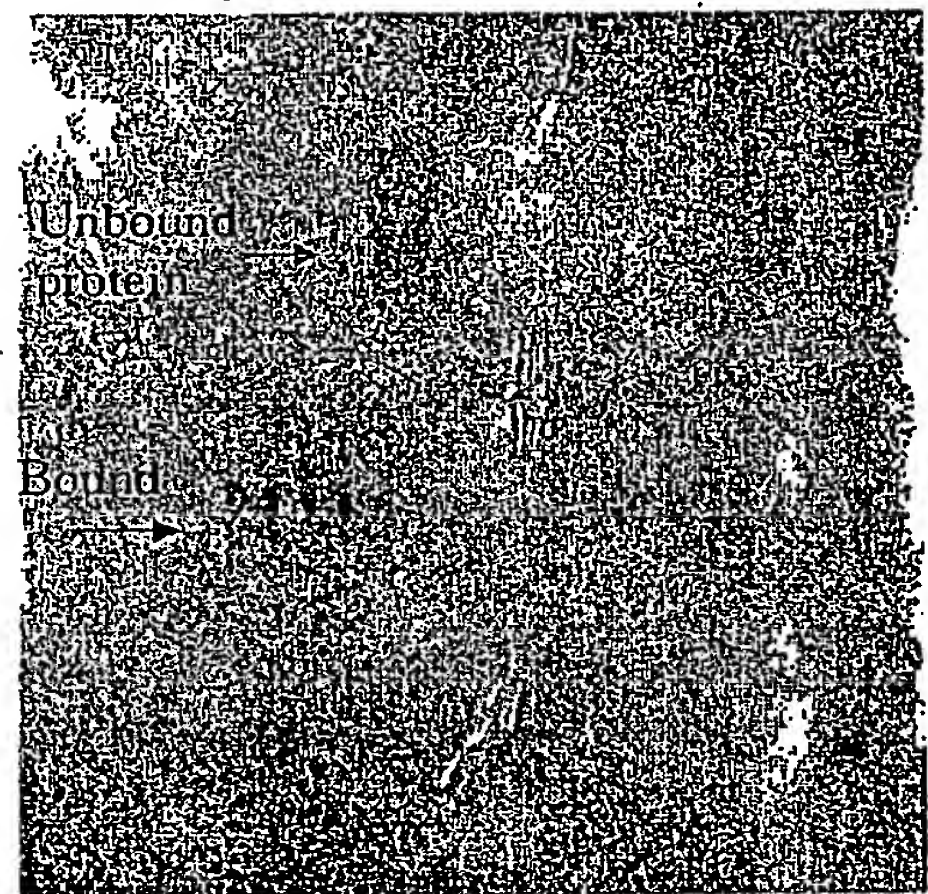


FIGURE 13

N-Acetyl Glucosamine Pathway

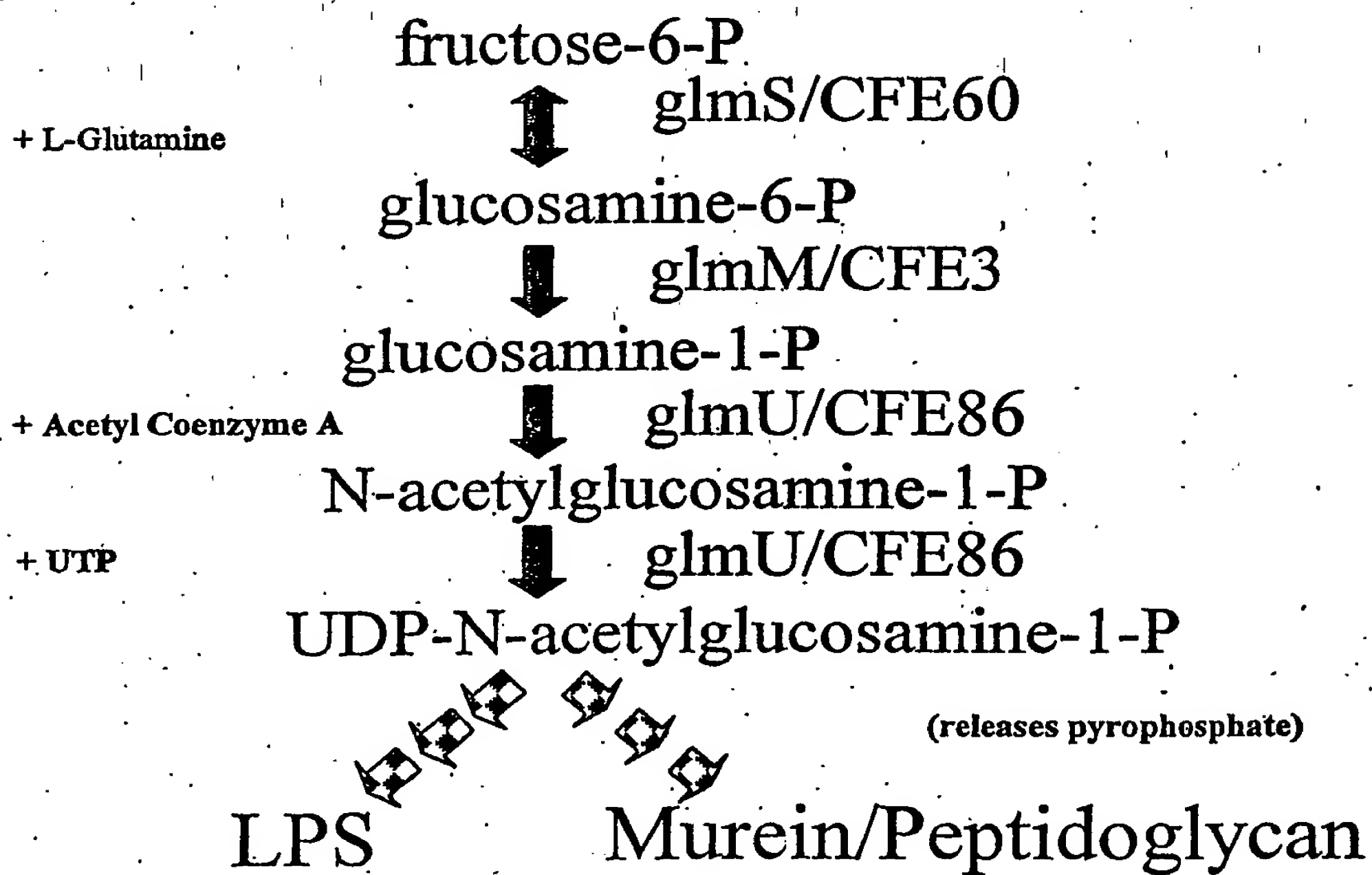


FIGURE 14

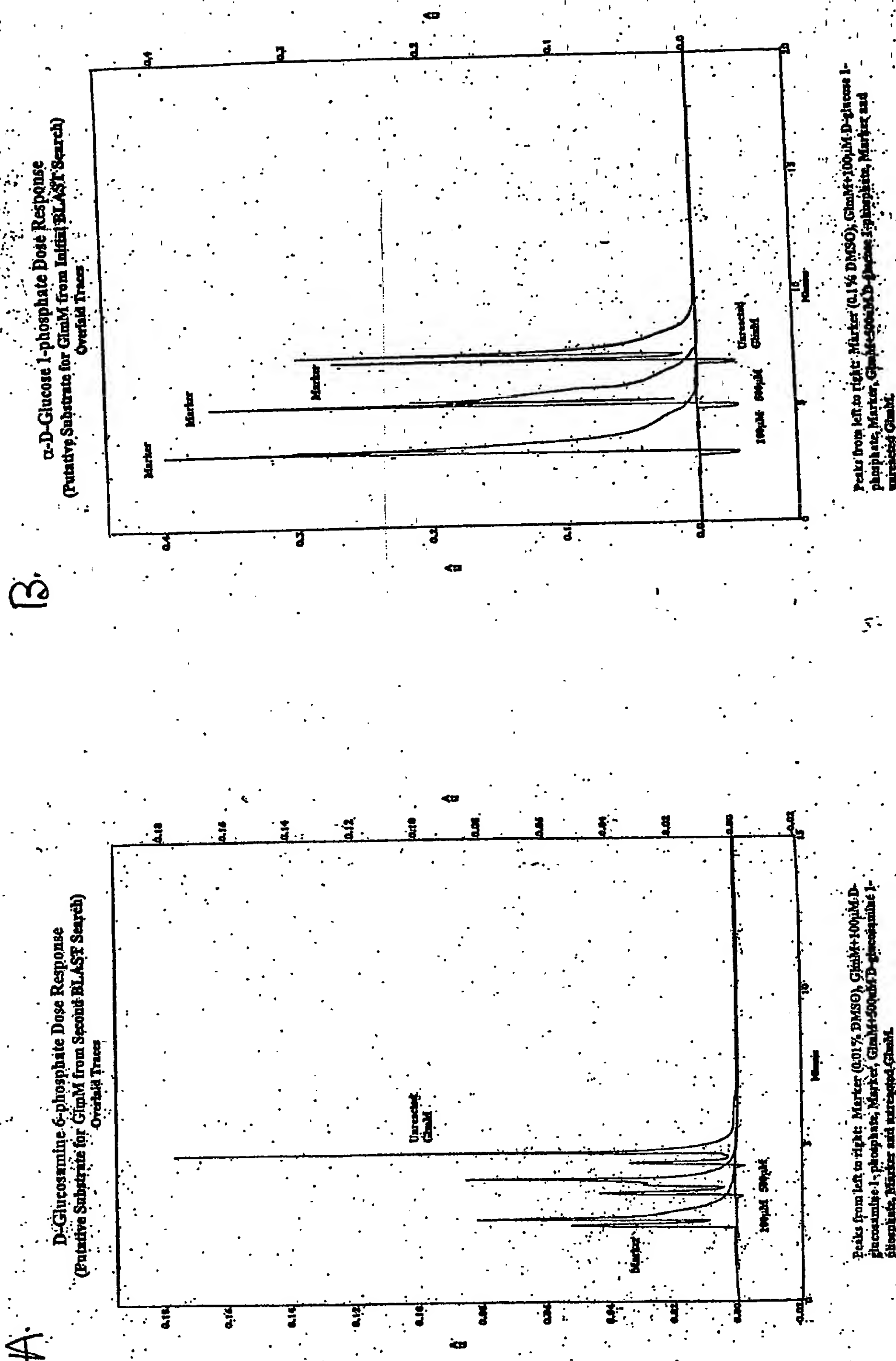


FIGURE 15

C:

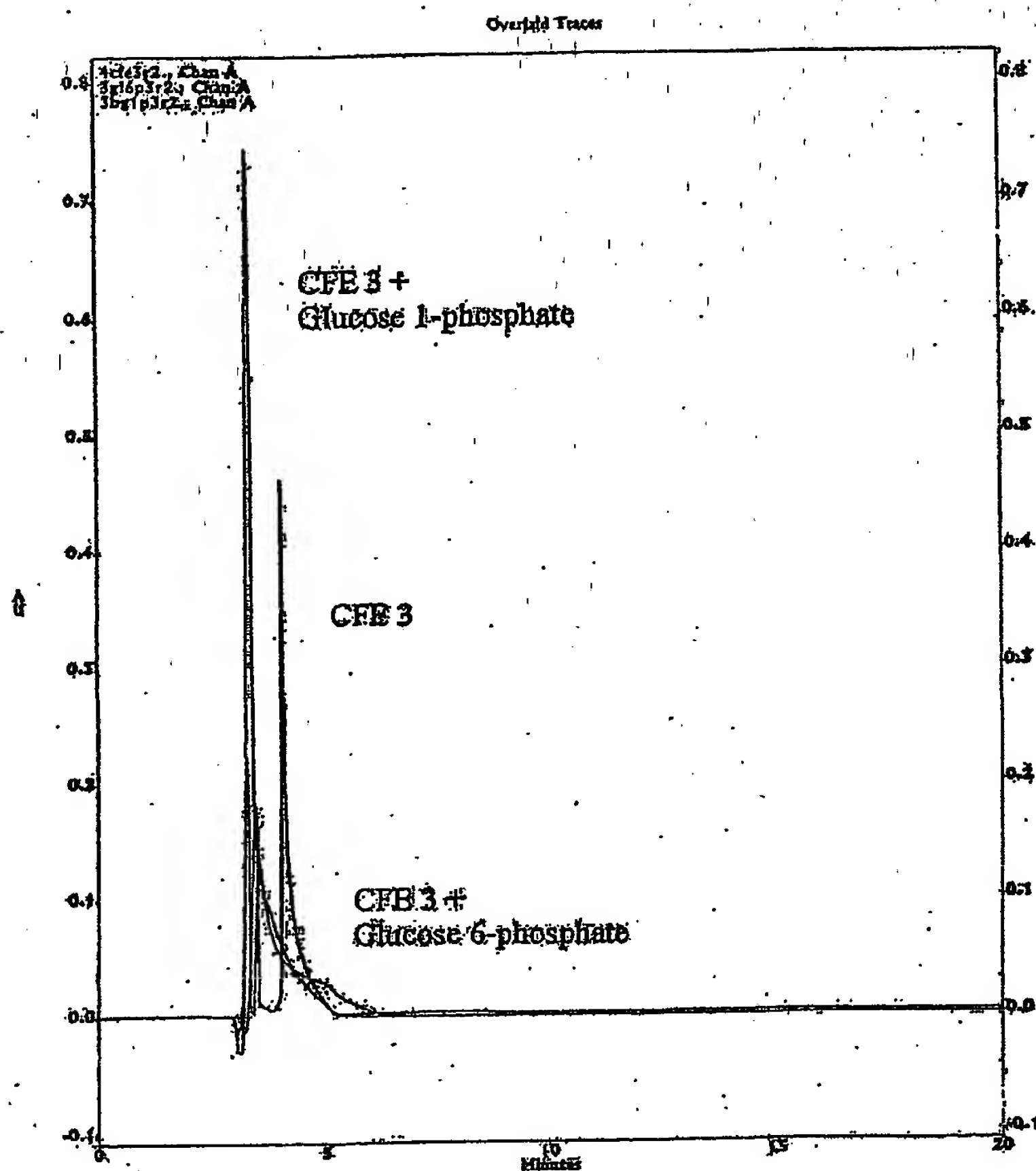


FIGURE 15

D.

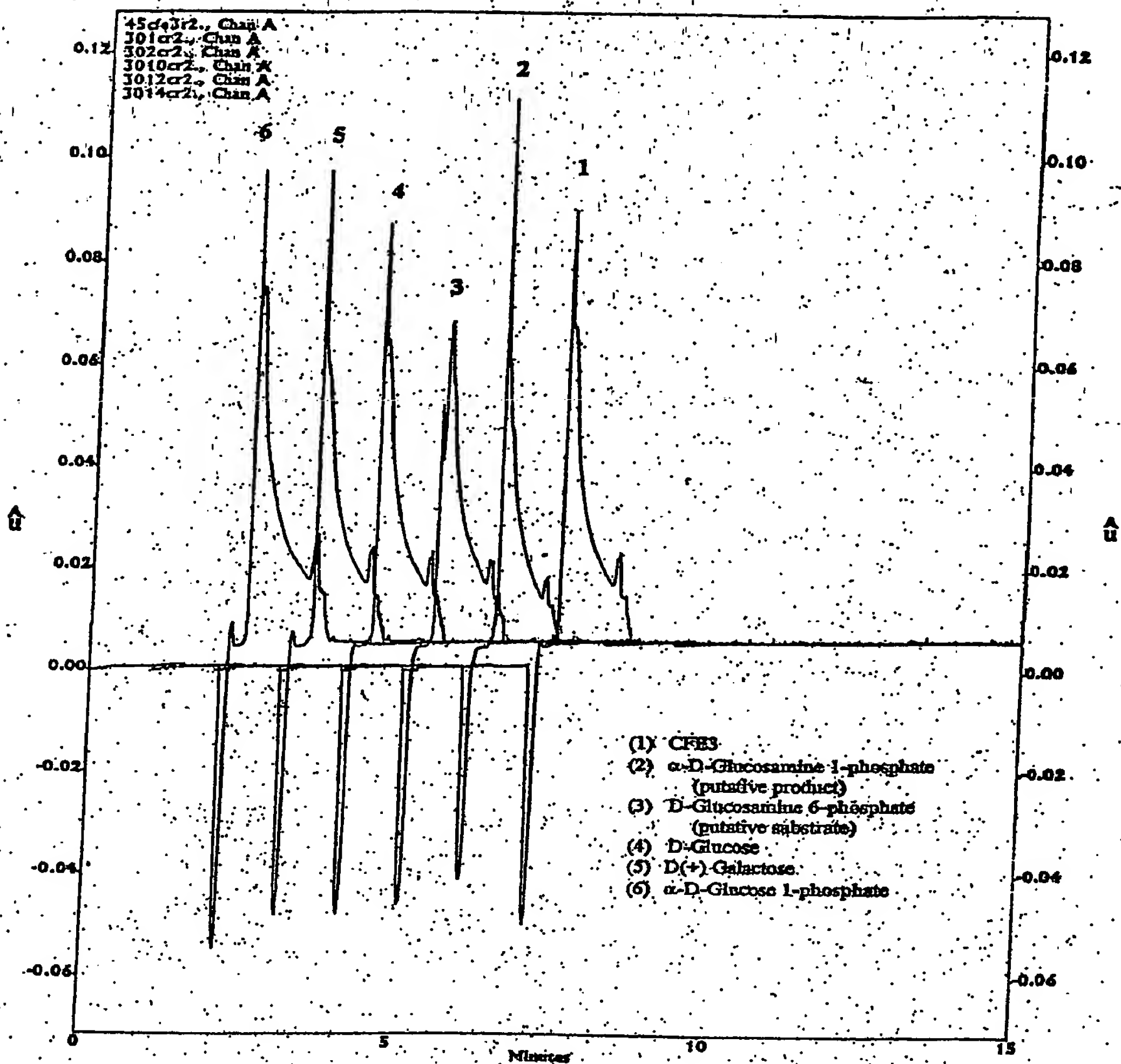


FIGURE 15

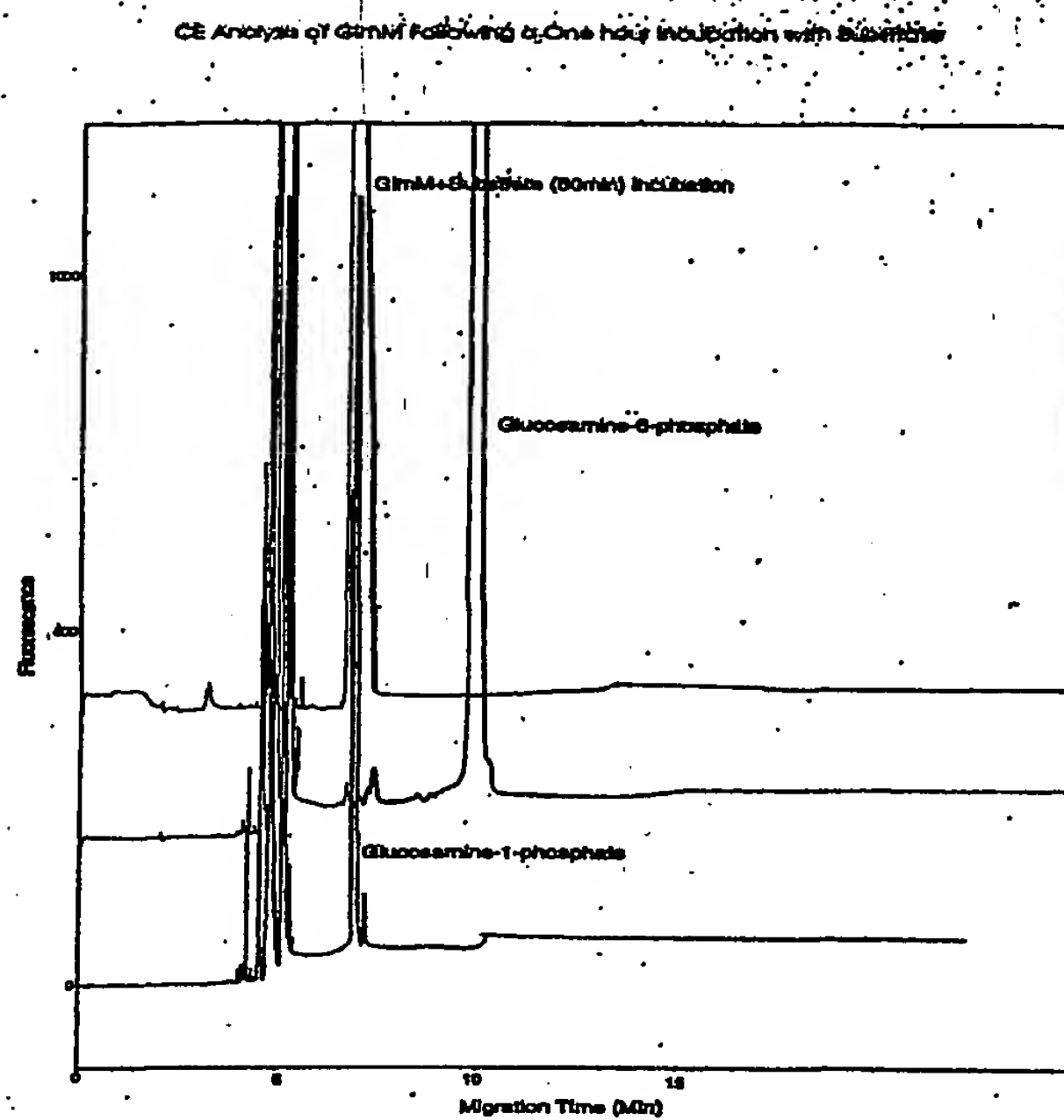


FIGURE 16

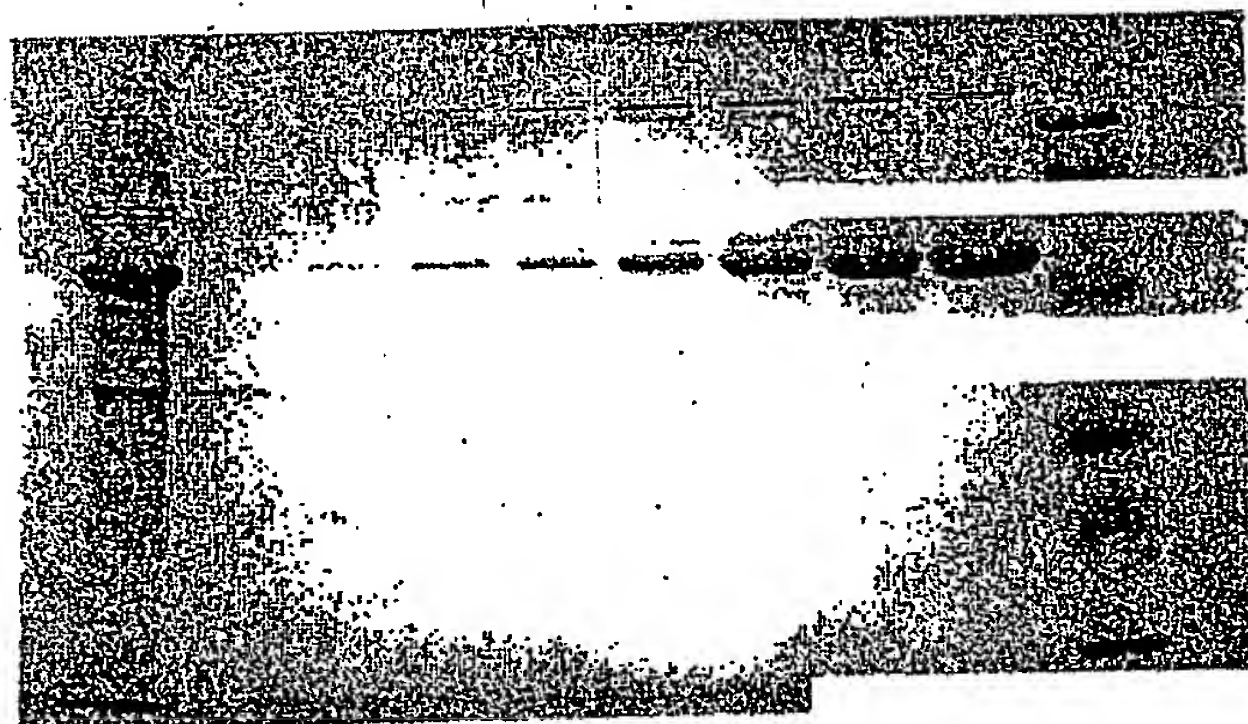


FIGURE 17

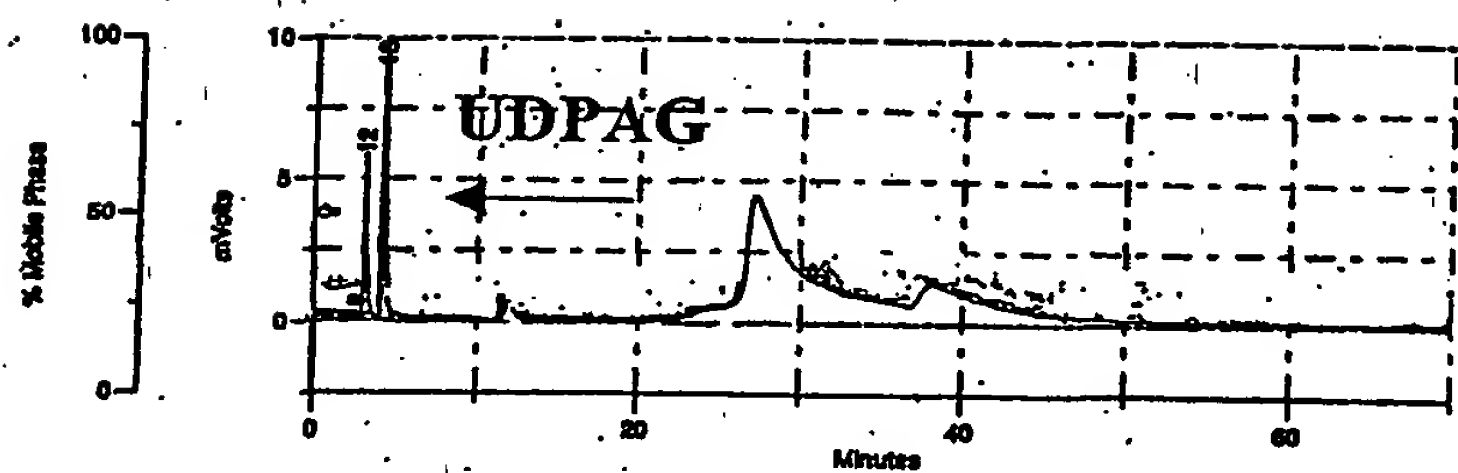


FIGURE 18

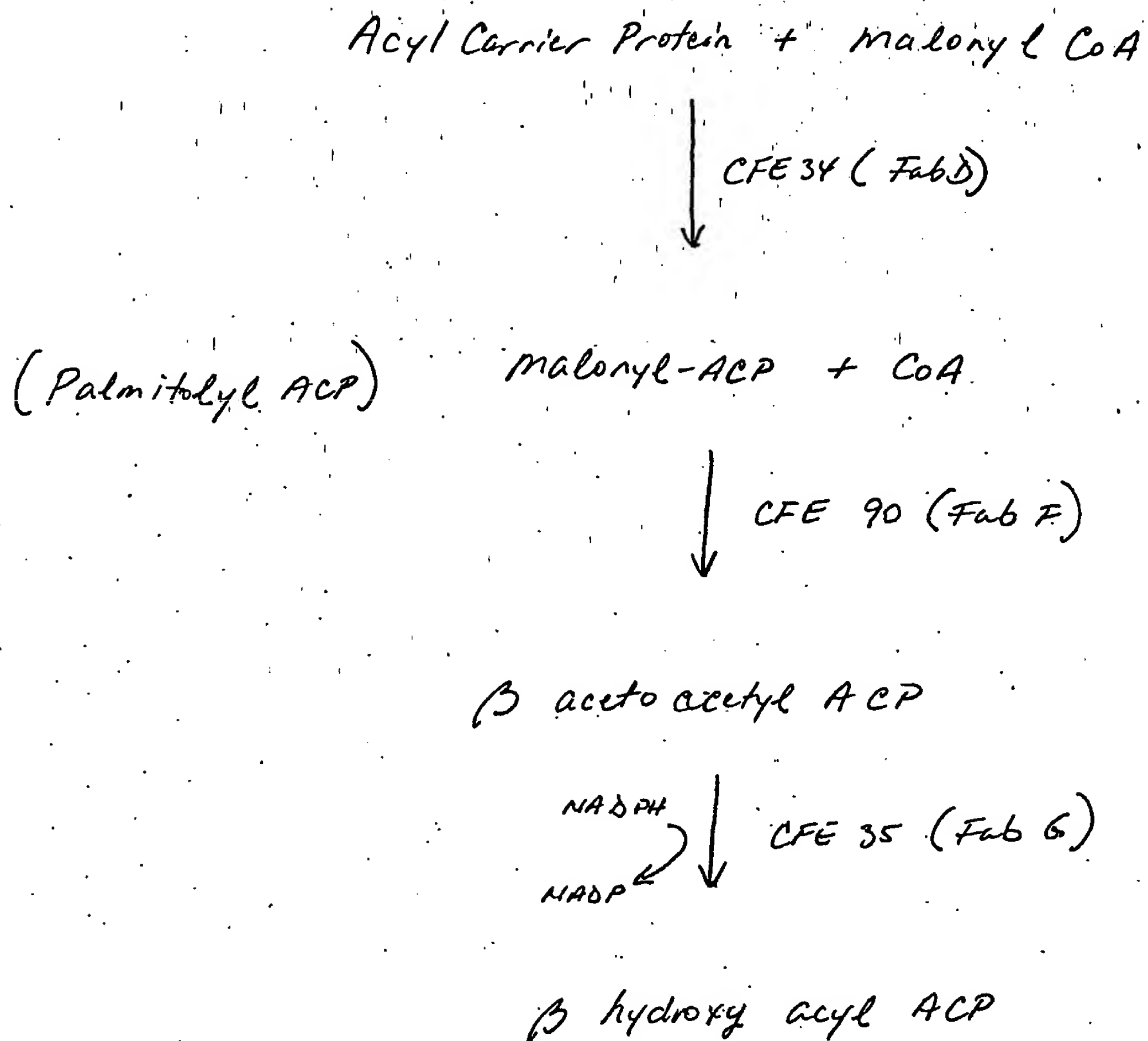


FIGURE 19.

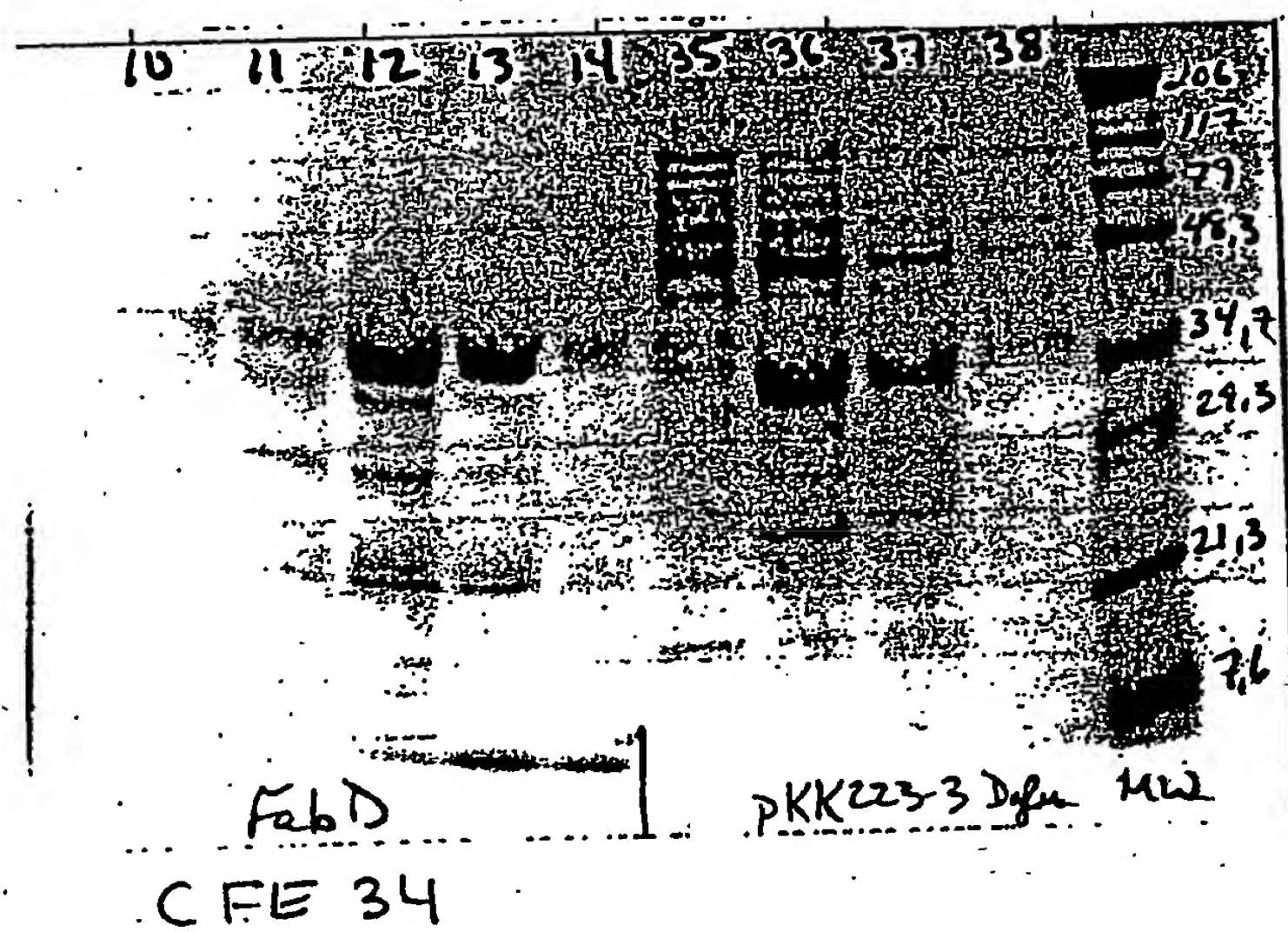


FIGURE 20

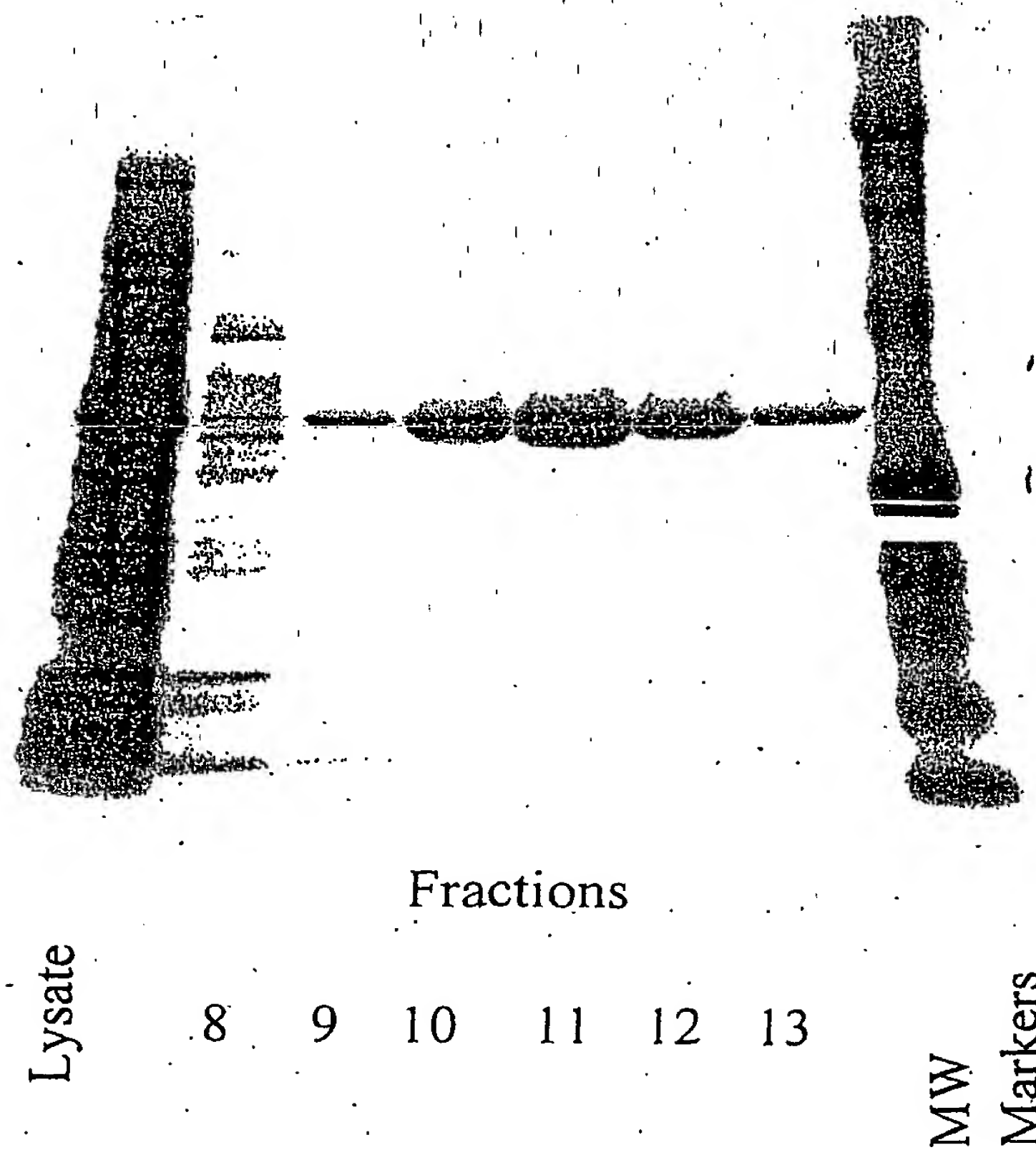


FIGURE 21

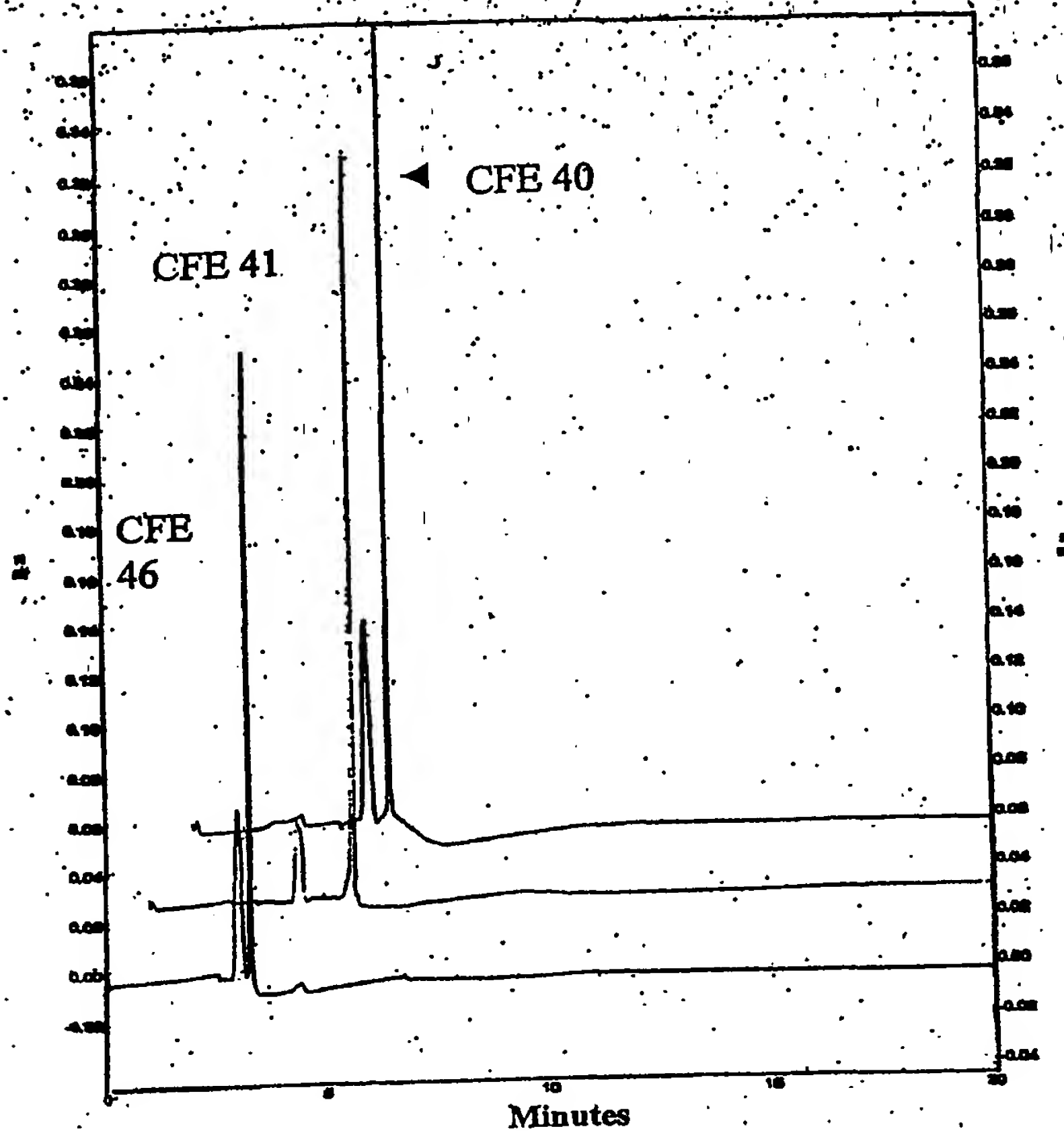


FIGURE 22

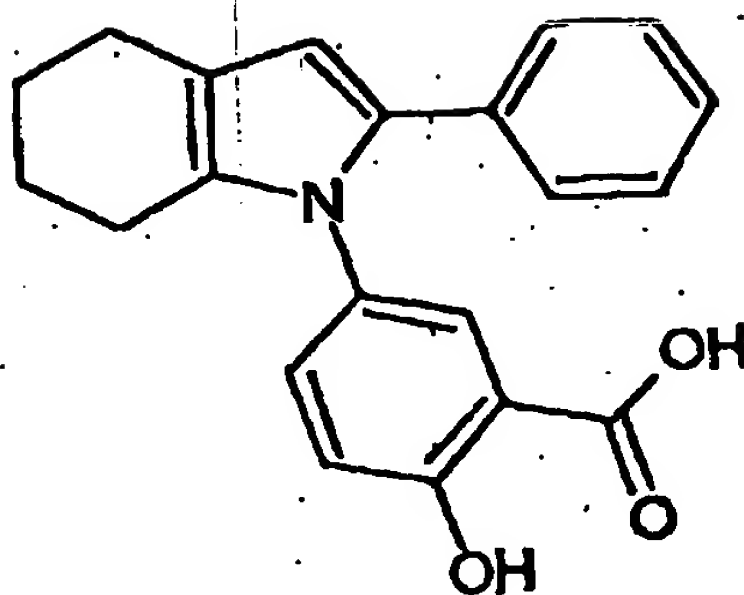


FIGURE 23

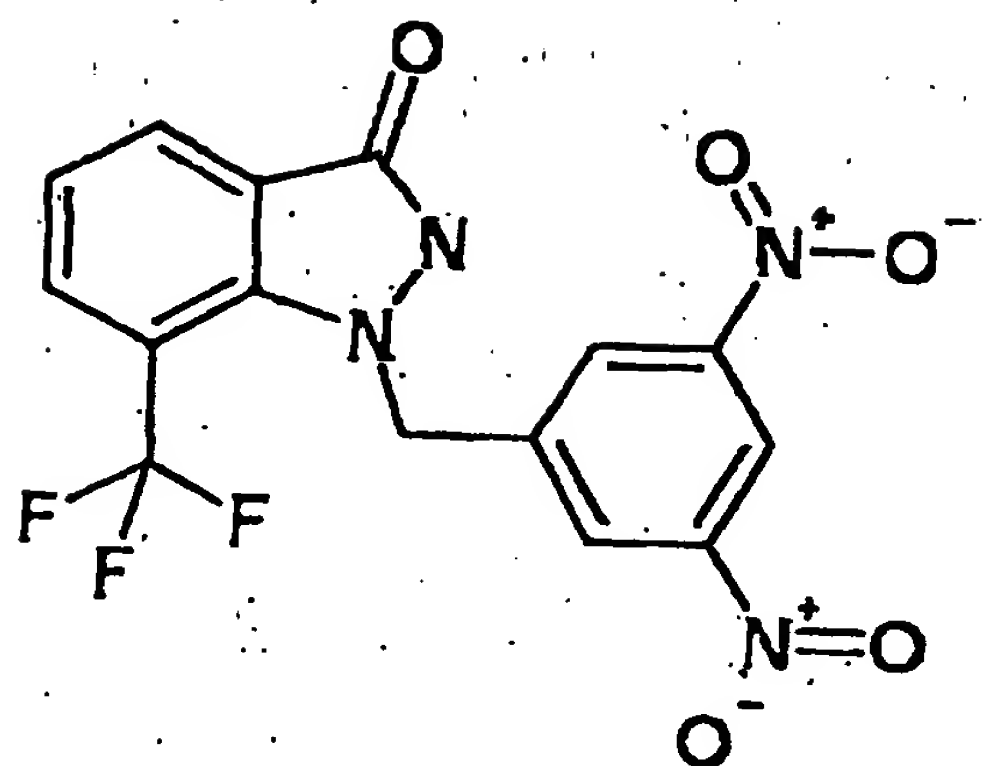


FIGURE 24

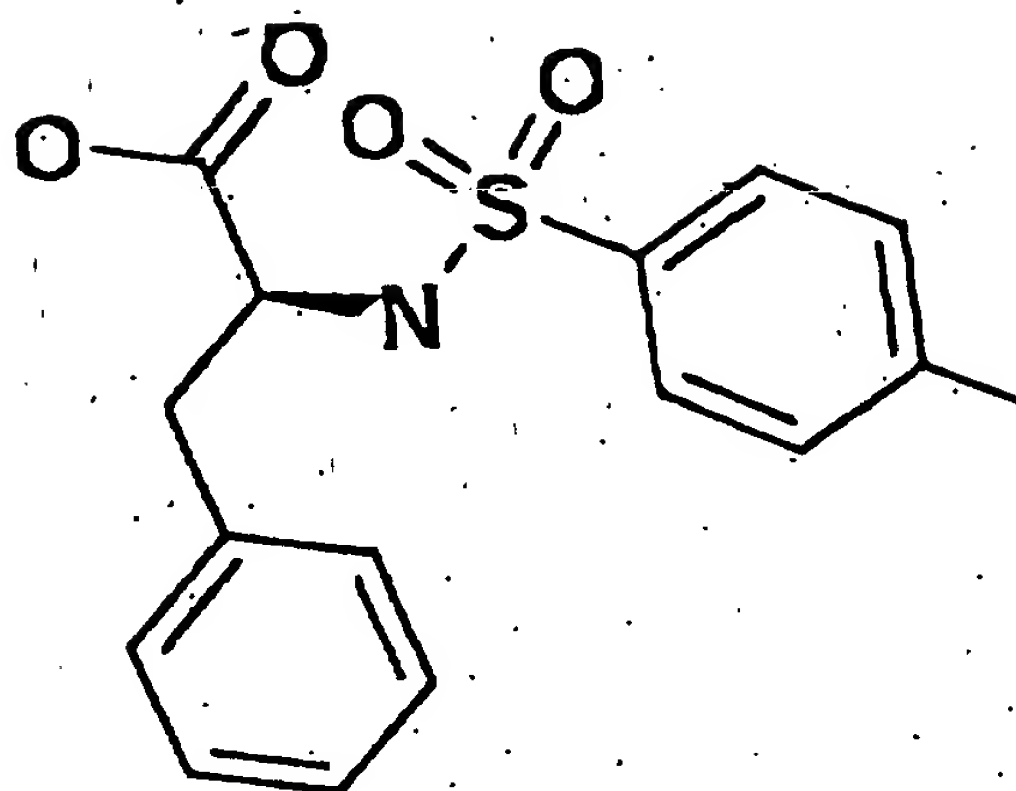


FIGURE 25

2 CFE1 "homologue of SEQ. ID NO. 1"

ATGATTATGCAGGAATTCTTGCCGGTGGAACTGGCACACGCATGGGGATCAGTAACCTTGCCAAAACAAT
 TTITAGAGCTAGGTGATCGACCTATTTTGATTTCATACAATTGAAAAATTNGTCTTGAGGCAAGTATTGAA
 AAAATTGTAGTTGGTGTTCATGGAGACTGGGTTTCTCATGCAGAAGATCTTGTAAGATAAATATCTTCCTCT
 TTATAAGGAACGTATCATCATTACAAAGGGTGGTGCTGACCGCAATACAAGTATTAAGAACATCATTGAA
 GCCATTGATGCTTATCGTCCGCTTACTCCAGAGGATATCGTTGTTACCCACGATTCTGTTCCGTCATTATT
 AACTTTCGCATGATTCAGGACAATATCCAATTGCCCCAAATCATGACGCAGTGGACACAGTGGTAGAA
 GCGGTTGATACTATCGTTGAAAGTACCAATGGTCAATTTATTACAGATATTCCAAATCGTGCTCACCTTTA
 TCAAGGACAAACACCTCAAACATTCCGTTGCAAGGACTTCATGGACCTTTATGGATCTCTTTCTGATGAA
 GAGAAAGGAAATCTTGACAGATGCATGTAAATCTTTGTGATCAAAGGAAAAGATGTGGCTTTGGCCAAA
 GGTGAATACTCAAATCTGAAGATTACAACCGTAACAGATTGGAAGATTGCAAAAAGTATGATTGAGAAA
 GACTAG

2 CFE2 "homologue of SEQ. ID NO. 2"

ATGGCTAACGTAATTATTGAAAAAGCTAAAAGAGAGAATGACCCATCTCACCAATCACTTGCTCGTGAAT
 TTGGTGCTATCCGTGCTGGTCTGCGCAATGCAAGCTTGCTTGACCGTGTACATGTAGAATACTATGGAGTC
 GAAACTCTCTTAACCAAATCGCTTCAATTACGATTCCAGAAGCGCGTGTGTTTGTGGTAACACCATTTGA
 CAAGTCTTCATTGAAAGACATCGACCGTGCTTGAACGCTTCTGATCTTGGTATCACACCGGCTAATGAC
 GGTCTCTGATTGCTTGGTTATCCAGCTCTTACAGAAGAAAGTCTGCTGACCTTGCTAAAGAAGTGA
 AGAAGGTGCGGCGAAAATGCTAAAGTGGCTGTCCGCAATATCCGTGCGGATGCTATGGACGAAGCTAAGA
 AACAGGAAAAGCAAAAGAAATCACTGAAGACGAATTGAAGACTCTTGAAAAAGATATTCAAAAAGTA
 ACAGACGATGCTGTTAAACACATCGACGACATGACTGCTAACAAAGAGAAAGAACTTTTGAAGTCTAA

2 CFE3 "homologue of SEQ. ID NO. 3"

ATGGGTAAATATTTGGGACTGATGGAGTCCGTGGGAGAAGCTAACCTAGAGCTAACACCAGAATTAGCCT
 ITAAACTAGGACGTTTGGAGGCTATGTTCTTAGTCAACATGAAACGGAAGCGCCGAAAGTCTTTGTAGG
 ACGTGACACACGTATTTAGGGGAAATGCTGGAATCGGCCCTGGTGGCAGGTCTCCTTTCAGTAGGGATT
 CAGGTATACAACTTGGTGTCTTGC AACACCAGCAGTAGCTTACTTGGTTGAAACTGAAGGAGCAAGTG
 CCGGTGTCATGATTTCTGCTAGCCACAACCCAGCCCTTGATAACGGAATCAAGTTCTTTGOCGGTGATGG
 CTTCAAACTAGATGATGAAAAAGAAGCAGAAATTGAAGCCTTGCTAGATGCTGAGGAAGACACTCTTCC
 TCGTCCAAGTGCAAGAGGCTTAGGAATTTTGGTAGATTATCCAGAAGGCTTGCGTAAGTATGAAGGATAC
 CTGTTTCAACTGGAACCTCTTGTATGGAATGAAGGTTGCCTTGGATACAGCTAATGGAGCAGCTTCTAC
 CACTGCCCGTCAAATCTTTGCAGACCTTGGTGCCCAATTGACGGTTATCGGGGAAACACCAGACGGTCTT
 AAGATCAACCTTAATGTTGGTTCAACACATCCAGAAGCCCTTCAAGAAGTGGTCAAAGAAAGTGGGTCA
 GCTATTGGTTTGGCCTTTGATGGAGACAGTGACCGCTTGATTGCTGTTGATGAGAATGGTGACATCGTCC
 ATGGTGACAAGATTATGTACATCATCGGAAAATACCTTTCTAAAAAAGGACAATTGGCTCAAAATACAAT
 TGTGACAACCTGTTATGTCTAACCTTGGTTTCCACAAGGCCTTGAATCGCGAAGGTATTAACAAGGCAGTT
 AQTGCAGTTGGTGACCGCTACGTTGTTGAAGAAATGAGAAAATCAGGTTACAACCTTGGTGGTGAACAGT
 CTGGTCACGTTATCTTGATGGATTACAATACCACAGGTGATGGTCAATTATCAGCAGTTCAATTGACTAA
 AATCATGAAGGAACTGGTAAGAGCTTATCAGAGTTGGCGGCAGAAAGTAACGATTTATCCACAAAATT
 AGTTAATATCCGAGTGGAAAACGTCATGAAGGAAAAGGCCATGGAAAGTGCCAGCTATCAAGGCCATCAT
 CGAGAAGATGGAAGAAGAAATGGCGGGGAACGGCCGTATCCTTGTTCGTCCAAGTGGAACAGAACCCCT
 CTGCGTGTTATGGCAGAAGCGCCTACAACAGAAGAAGTAGACTACTATGTTGATACCATCACAGATGTA
 GTTCGTGCTGAAATTGGGATTGACTAA

2 CFE4 "homologue of SEQ. ID NO. 4"

2 CFE 4 homologue of SEQ ID NO: 4

Fig. 29

ATGAA AAAAATACTAATTGTAGATGATGAGAAACCAATCTCGGATATTATCAAGTTTAATATGACCAAGG
 AAGGTTATGAAGTTGTAACCTGCTTTTAATGGTCGTGAAGCGCTAGAGCAATTTGAAGCAGAGCAACCAGA
 TATTATTATTCTGGATTGTGATGCTTCCAGAAATTGATGGTTTGAAGTTGCTAAGACCATTCGTAAGACAA
 GCAGTGTGCCCATTCCTTATGCTTTCAGCCAAAGATAGTGAATTTGATAAGGTTATCGGTTTGGAACTTGGG
 GCAGATGACTATGTAACGAAACCCCTTCTCCAATCGTGAGTTGCAGGCGCGTGTTAAAGCTCTTCTGCGTC
 GTTCTCAACCTATGCCAGTAGATGGTCAGGAAGCAGATAGTAAACCTCAACCTATCCAAATTGGGGATT
 AGAAATTGTTCCAGACGCTACGTGGCTAAAAAATATGGCGAAGAAGTACTTAACCCATCGTGAATTT
 GAGCTTTTGTATCATTAGCACCGCATAACAGGTCAAGTCATCACGCGCGAACACTTGCTTGAGACTGTCT
 GGGGTATGACTATTTTGGTGATGTCCGCACAGTTGATGTGACTGTACGACGCTCTCGTGAGAAGATTGA
 AGATACGCCAGCCGACCAGAGTATATCTTGACGCGCGGTGGTGTAGGGTATTACATGAGAAATAATGCT
 TCA

Fig. 30

2 CFE5 "homologue of SEQ. ID NO. 5"

ATGGAAGAAATCTCTGTATTGGTTGTGGAGCAACCATTGACACGACAGATAAGGCTGGTCTTGGTTT
 CCCCCAGTTGGCAGTTGAAAAAGGTTTGGAGACTGGCGAAGTCTATTGCCAACGCTGTTTCCGTCCTCG
 CCACTACAATGAAATCACAGATGTCCAGTTGACGGACGATGATTTCTCAAGCTCTTGACAGAGGTGGGA
 GACAGTGATGCTTAGTGGTCAATGTCAATTGATATCTTTGATTTTAATGGATCTGTATCCAGGTTTACC
 AGGTTTCGTCTCGGGCAATGATGTCTCTTGGTAGGAAATAAAAAAGATATCCTTCTAAGTCAGTTAAG
 TCTGGTAAGATTAGCCAGTGGCTCATGAACGTCGCCATGAAGAAGGTCTTCGTCCAGTCGATGTGGTCC
 TAACTTCAGCACAATAAATATGCCATTAAGGAAGTCATTGATAAGATTGAACACTACCGTAAGGGCC
 GCGATCTCTATGTGGTGGTGTGACCAACGTTGGAAAAATCAACTCTAATCAATGCTATTATCCAAGAAAT
 CACGGGTGATCAGAATGTCACTACTTCAAGCTTTCCAGGGACAACCTTGGACAAAATAGAGATTCCG
 CTGACGACGGATCTTATATTTACGATACGCCGGGAATTATCCACCGCCACCAGATGGGCTCACTACTTGA
 CGGCCAAAAACCTCAAGTATGTCACTCTAAAAAGGAAATCAAGCCTAAGACCTATCAGCTTAATCCTGA
 GCAAAACCTATTTTTAGGTGGTTTGGGACGCTTTGACTTTATAGCAGGAGAAAAGCAAGGATTACTGCT
 TTCTTTGATAATGAACCTCAACTCCATCGTAGCAAGCTTGAAGGAGCTAGTGCTTTCTACGATAAGCACC
 TGGGAACCTCTCTGACACCACCAATAGCAAGGAAAAAGAAAGATTTCCTAAGGCTAGTCCAGCATGTCTT
 TACCATTAAGATAAGACAGACCTAGTCATTTACGGCCTAGGCTGGATTCTGTGTAACAGGCATAGCAAAA
 GTCGCCGTCTGGGCACCAGAAGGCGTCGCCGTCTGTCACACGAAAAGCAATTATTTAA

Fig. 31

2 CFE6 "homologue of SEQ. ID NO. 6"

ATGATCCAGATGATAGTTTGACATTGCACACGGACTTGTACCAGATCAACATGATGCAGGTTTACTT
 ACCAAGGGATTACAAATAAGAAGGCGGTCTTTGAGGTGTATTTCCGCCAACAGCCTTTTAAGAACGGCTA
 TGGCGTTTGTGAGGTTTGGAAAGAATTGTGAACCTATCTTGAAGACTTGGCTTTTTCAGATAGTGATATAG
 CCTATTGGAGTCGCTTGGTTATCATGGGGCGTTCTTGGATTACCTTCGCAATTTCAAGTTGGAGTTGACC
 GTTCGTCTGCCCCAAGAAGGGGATTTGGTTTGTGCTAATGAACCGATTGTGCAGGTGGAAGGACCTCTAG
 CCAATGTGAGTTGGTCGAAACGGCTCTTTTGAACATCGTCAACTACCAGACCTTGGTGGCGACGAAGGC
 AGCTCGTATTCGTTCCGTTATCGAAGATGAACCTTGTATGGAGTTTGGGACACGTCGGGGCTCAAGAAATG
 GATGCGGCCATCTGGGGAACACGCGCAGCTGTGATTGGTGGCGCCAATGGAACCAAGCAACGTGCGTGGC
 GGTAAAGCTCTTTGACATTCTGTGTTTGGGAACCCATGCCCATGCCCTTGGTACAGGTTTATGGCAATGACTA
 TGAAGCTTCAAGGCTTACGCTGCGACCCACAAAAATTGTGTCTTTCTTGTGGATACCTATGACACCCTTC
 GCATCGGTGTACAGCTGCCATTGAGGTGGCGCGTGAGCTGGGTGATTAGATTAACTTTATGGGTGTGCG
 GATTGACTCTGGGATATTGCTTACATTTCTAAGAAAGTCCGTCAGCAACTGGACGAGGCTGGATTTACA
 GAGGCTAAGATTATGCTTCTAATGATTTGGACGAAAAATACTATCTCAACCTCAAGATGCAAAAGGCCA
 AGATTGATGTCTGGGGCGTGGGTACCAAGCTGATTACAGCCTATGACCAGCCAGCTCTTGGGGCGGTTTA
 CAAGATTGTTGCAATCGAAGATGAAACTGGTCAGATGCGCAATACGATTAAAGCTGTCTAATAATGCGGA
 AAAAGTGTGACGCCAGGTAAGAAGCAAGGTGTGGCGCATTACCAGTCGTGAAAAAGGCAAGTCAGAAG
 GTGACTACATCACTTATGATGGTGTGGATATTAGCGACATGACAGAAATCAAGATGTTCCATCCGACCTA
 TACATAATCAAGAAGACGGTTCGTAATTTGATGCCGTTCTCTCTTGGTGGATATCTTCAAAGAAGGTA
 TATTAGTTTACAACCTGCTAGTTTGAAGTACATTGAGGATTATGCCCGTAAGGAATTTGACAAGTTGTGG
 GATGAGTATAAGCGTGTGCTCAATCCGCAGCACTATCCAGTGGATTGCGCGCGTGATGTATGGCAAGATA
 AGATGGACTTGATTGATAAGATGCGCAAGGAAGCCCTTGGTGAAGGAGAAGAAGATGA

Fig. 32

2 CFE7 "homologue of SEQ. ID NO. 7"

ATGGCTACTATTCAATGGTTTCTGGTCAATGTCTAAAGCGCGTCGACAGGTGCAGGAAAATTTAAAT
 TTGTTGATTTTGTGACGATTTTAGTAGATGCACGCTTGCCTCTATCTAGTCAAAATCCTATGTTGACCAAG

2CFE 7 (cont'd)

ATTGTTGGTGATAAACCACAACTCTTGATTTTAAACAAGGCCGACTTGGCTGATCCAGCAATGACCAAGG
 AATGGCGTCAGTATTTTGAATCACAAGGAATCCAGACGCTAGCTATCAACTCCAAAGAGCAAGTGACTGT
 AAAAGTTGTAACAGATGCGGCCAAGAAGCTCATGGCTGATAAGATTGCTCGCCAGAAAGAACGTGGGAT
 TCAGATTGAAACCTTGCGTACCATGATTATCGGGATTCCAAACGCTGGTAAATCCACTCTGATGAACCGT
 TTGGCTGGTAAAAAGATTGCTGTGTTGGAAACAAGCCAGGGGTCACAAAAGGTCAACAATGGCTTAAA
 ACCAATAAAGATCTGGAAATCTTGGATACACCGGGGATTCTCTGGCCTAAGTTTGAGGATGAAACTGTTG
 CACTTAAGTTGGCATTGACTGGAGCTATCAAGGATCAGTTGCTTCCTATGGATGAGGTTACCATTTTTTGGT
 ATCAATTATTTCAAAGAACATTATCCAGAAAAGCTGGCTGAACGCTTCAAACAAATGAAAATTGAAGAA
 GAAGCGCCTGTGATTATTATAGATATGACCCGCGCCCTCGGTTTCCGTGATGACTATGACCGTTTTTACAG
 TCTGTTGCTGAAGGAAGTCCGTGATGGCAAACCTCGGTAACCTATACCTTAGATACATTGGAAGACCTCGAT
 GGCAACGATTAA

2CFE8 "homologue of SEQ. ID NO. 8"

ATDATTACAATGTTGTACTTGTAGGGCGTATGACACGTGACGCTGAGTTGCGTTATACCCCATCAAATG
 TAGCAGTTGCGACTTTTACTCTTGCAGTAAACCGTACATTTAAGAGTCAAAATGGTGAACGTGAGGCTGA
 TTTATCAATGTCGTTATGTGGCGCCAACAGGCTGAAAATCTTGCTAACTGGGCTAAAAAAGGCTCACTT
 ATCGGGGTGACAGGTCGTATCCAGACTCGTAGTTACGATAACCAGCAAGGACAACGTGTCTACGTGACA
 CAGGTCGTGGCTGAGAAATTTCAAATGTTGGAAAGCCGTAGTGTGCGTGAGGGTCACACAGGTGGAGCT
 TACTCTCACCAACTGCAAACCTATTACGACCTACAAATTCAGTACCAGACTTTTCACGTAATGAAAATC
 CATTTCAGCAACAAACCCATTGGATATTTTCAGATGATGATTACCATTCTAA

2CFE9 "homologue of SEQ. ID NO. 9"

ATGAAAACGCGTATTACAGAATTATTGAAGATTGACTATCCTATTTTCCAAGGAGGGATGGCCTGGGTTG
 CTGATGGTGATTTGGCAGGGGCTGTTTCCAAGGCTGGAGGATTAGGAATTATCGGTGGGGGAAATGCCCC
 GAAAGAAGTTGTCAAGGCCAATATTGATAAAATCAAATCATTGACTGATAAACCCTTTGGGGTCAACATC
 ATGCTCTTATCTCCCTTTGTGGAAGATATCGTGGAATCTCGTTATTGAAGAAGGTGTTAAAGTTGTCACAAC
 AGGAGCAGGAAATCCAAGCAAGTATATGGAACGTTTCCATGAAGCTGGGATAATCGTTATTCCTGTCGTT
 CCTATCTCGCTTTAGCTAAACGCAATGGAAAAATCGGTGCAGACGCTGTTATTGCAGAAGGAATGGAA
 GCTGGGGGGCATATCGGTAAATTAACAACCATGACCTTGGTGCGACAGGTAGCCACAGCTGTATCTATTC
 CTGTTATTGCTGCAGGAGGAATTGCGGATGGTGAAGGTGCTGCGGCTGGCTTTATGCTAGGTGCAGAGGC
 TGTACAGGTGGGGACACGGTTTGTAGTTGCAAAAAGAGTCGAATGCCCATCCAAACTACAAGGAGAAAT
 TTTAAAAAGCAAGGGAATATTGACACTACGATTTTCAGCTCAGCACTTTGGTCATGCTGTTGCTGCTATTA
 ATCAGTTGACTAGAGATTTTGAAGTGGCTGAAAAAGATGCCCTTAAGCAGGAAGATCCTGATTAGAAAT
 CTTTGAACAAATGGGAGCAGGTGCCCTAGCCAAAGCAGTTGTTCAAGGTGATGTGGAGGGTGGCTCTGTC
 ATGGCAGGTCAAATCGCAGGGCTTGTCTTAAAGAAGAAACAGCTGAAGAAATCCTAAAAGATTGTATT
 ACGGAGCCGCTAAGAAAATTCAAGAAGAAGCCTCTCGGTGGACAGGAGTTGTAAGAAATGACTAA

2CFE10 "homologue of SEQ. ID NO. 10"

ATGATCCATATTCAAGGAATCAAAGAAGCTCTTCCCCACCGTTATCCTATGCTTCTAGTGGACCGTGTCTT
 GGAAGTGAGCGAGGATACCATTTGTTGCTATCAAAAATGTGACCATTAAACGAACCTTTCTTTAACGGCCAC
 TTTCTCAATACCCAGTTATGCCAGGTGTTCTGATTATGGAAGCCTTGGCGCAAACCTGCTGGTGTGTTGGA
 GTTATCAAACCTGAAAAATAAGGAAAAACTGGTCTTTTACGCTGGTATGGACAAGGTAAAGTTCAAGAA
 GCAAGTTGTACCAAGCGACCAATTGGTTATGACAGCGACTTTTGTAAAACGTCGTGGCACCATAGCTGTG
 GTTGAAGCAAAGGCTGAAGTGGATGGCAAGCTTGACGCCAGTGGTATCCTTACTTTTGAATTGGGAACT
 AA

2CFE11 "homologue of SEQ. ID NO. 11"

ATGATTAAATCAAATTTATCAACTAACTAAGCCTAAGTTTATCAATGTCAAATATCAGGAAGAGGCTATTG
 ACCAAGAGAATCATATCCTTATCCGTCCCACTACATGGCTGTCTGTGATGCGGATCAGCGTTACTATCA
 GGCAAAACGTGATCCCAAGATTTTGAATAAAAAGCTTCCAATGGCAATGATTACAGGATCATGTGGAAC
 CGTCAATTTCTGACCCGACCGGAACCTACGAGGTTGGTCAAAAAGTTGTGATGATTCCTCAATCAGTCTCCT
 ATGCAGAGTGATGAAGAAATCTATGAAAACCTACATGACAGGGACCCATTCTTGTCTAGTGGATTGATG
 GCTTTATGAGAGAGTTTGTCTCTCCCTAAAGATCGTGTGGTGGCTTATGATGCTATTGAAGATACGGTT
 GCAGCCATTACAGAGTTTGTGAGTGTGGGCATGCACGCTATGAATCGTCTATTGACTCTTGCTCATAGCA
 AGCGGGAGCGGATCGCCGTTATTGGAGATGGAAGTTTAGCTTTTGTGGTTGCCAATATTATCAACTATAC
 TTTGCCAAGAGCAGAGATTGTGGTTATTGGTCTGATTTGGGAAAAGTTGGAACCTCTTCTCATTGGCCAAA

2 CFE 11 (Contd.)

Fig. 36 (Contd.)
GAATGGTATATTACGGATAATATTCCTGAAGATTGGCCTTTGACCATGCTTTTGAATGTGTGGTGGTGA
TGGTACTGGACCAGCTATTAATGACTTGATTGCTACATTCGTCCTCAGGGAACGATTCTCATGATGGGA
GTTAGCGAATATAAAGTCAATCTCAATACTCGCGATGCCTTAGAAAAGGGCTTGATTTTGGTTGGGTCAT
CTCGTTCTGGTCCGATTGATTTTGA AAAATGCTATCCAAATGATGGAAGTCAAGAAATTTGCCAATCGTCTT
AAAAATATCCTTTATCTAGAAGAACCTGTAAGAGAAATTAAGATATTCATCGTGTCTTTGCAACCGATT
TAAACACAGCCTTTAAACAGTGTTTAAGTGGGAAGTATAA

2 CFE12 "homologue of SEQ. ID NO. 12"

Fig. 37
ATGAACCTAA AACTACTTTTGGGCCTTCTTGCTGGGCGTCTTCCCACTTCGTTTAAAGCCGTCTTGGACG
TGAAAGTACGCTCCAGGGAAAGTCGCCCTTCAATTTGATAAAGATATTTTACAAAGCCTAGCTAAGAAG
TACGAGATTGTGCTTGTCACTGGAACAAATGGAAAAACCCTGACAACCTGACCTGTCGGCATTTTAA
AAGAGCTTTATGGTCAAGTTCTAACCAACCCAAAGCGGTGCCAACATGATTACAGGGATTGCAACAACCTT
CCTAACAGCCAAATCTTCAAAAACCTGGGAAAAATATTGCCGTCTCTCGAAATTGACGAAGCCAGTCTATCT
CGTATCTGTGACTATATCCAGCCTAGTCTTTTGTGCTACTAATACTTCCGTGACCAGATGGACCGTTTC
GGTGAAATCTATACTACCTATAACATGATATTGGATGCCATTTCGAAAAGTTCCAACCTGCTACTGTTCTCCT
TAACGGAGACAGTCCACTTTTCTACAAGCCAACTATTCCAAACCTATAGAGTATTTTGGTTTGGACTTGG
AAAAAGGACCAGCCCAACTGGCTCACTACAATACCGAAGGGATTCTCTGTCTGCTGCTGCAAGGCATCCT
CAATAATGAGCATAATACCTATGCAAACCTTGGGTGCCTATATCTGTGAAGGTTGTGGATGTAAACGTCCT
GATCTCGACTATCGTTTGACAAAACCTGGTTGAGTTGACCAACAATCGCTCTCGCTTTGTGCTAGACGGCC
AAGAAATACGGTATCCAAATCGGCGGGCTCTATAATATCTATAACGCCCTAGCTGCTGTGGCCATCGCCCC
TTTCTAGGTGCGGATTTCGCAACTCATCAAACAGGGATTGACAAGAGCCGTGCTGTCTTTGGACGCCAA
GAAACCTTTCTATCGGTGACAAGGAATGTACCCTTGTCTTGATTAAAAATCCAGTCCGGTGCAACCCAAAG
CTATCGAAATGATCAAACTAGCACCTTATCCATTTAGCCTATCTGTCTCTCTTAATGCCAACTATGCAGAT
GGAATTGACACTAGCTGGATCTGGGATGCAGACTTTGAACAAATCACTGACATGGACATTCTGAAATCA
ACGCTGGCGGTGTTCTGTCATTCTGAAATCGCTCGCTCGCTCCGAGTGACTGGCTATCCAGCTGAGAAAAT
CACTGAAACGAGTAATCTGGAGCAAGTTCTCAAGACCATTGAGAATCAAGACTGCAAGCATGCCTATATT
CTGGCAACTTATACTGCCATGCTGGAATTTCTGTAAGTCTGGCTAGTCTGTCAGATTGTTAGAAAGGAGA
TGAACCTAA

2 CFE13 "homologue of SEQ. ID NO. 13"

Fig. 38
ATGGTTTATACTTCACTTTCTCTCAAAAAGATGGCAATTACCCCTATCAGCTCAACATTGCCACCTCTACGG
AAATCTCATGAATACCTACGGGGGACAATGGAAACATCCTCATGCTCAAGTATGTGGCTGAAAAACTGGG
AGCCCATGTGACCGTTGACATCGTTTCTCTCCATGATGACTTTGATGAAAATCACTACGACATCGECTTTT
TCGTTGGTGGTCAAGACTTTGAACAAAGTATCATTGACAGACGACCTACCTGCTAAAAAAGAGAGCATTG
ACAACCTACATCCAAAACGACGGTGTAGTTCTGGCTATCTGCGGTGGTTTCCAACCTATTGGGTCAATATTAT
GTTGAAGCTTCAGGAAAACGTATCGAAGGGCTAGGGGTGATGGGACACTACACGCTCAACCAGACCAAT
AACCGTTTATCGGTGACATCAAGATTCACAATGAAGATTTGATGAAACCTACTATGGATTGAAAATC
ACCAAGGCCGTACCTTCTCTCTGATGACCAAAAACCGCTGGGACAGGTTGTCTATGGAAATGGAAACAA
CGAAGAAAAGGTGCGGTGAAGGGGTTTATTATAAGAATGTCTTTGGTTCTACTTCCACGGGCCTATCCTC
TCTCGTAATGCCAATCTGGCTTATCGCCTAGTTACTACTGCCCTCAAGAAGAAATATGGTCAGGACATCC
AACTCCCTGCCTATGAGGATATCCTCAGCCAAGAAATCGCTGAAGAGTACAGTGACGTCAAAAGCAAGG
CTGACTTTCTTAA

2 CFE14

Fig. 39
ATGAATCTAAAGAAAATACAGAACTTGTTTTTCGAGAAGTTGCAGAGGCTAGTCTGAGTGCTCATCGAG
AGAGTGGTTCTGGTCTCTGTGCTATGCAAGTATGTAGATGTACCGACAGCGGAAGCCTTCTCTCC
GCTAGGTGTTCTCATATCGGTGAAAATCGTGTAGATAAGTTTCTGGAAAAATATGAAGCTTTAAAGAT
COAGATGTGACTTGGCATTGATTGGTACCTTGCAAAGACGTAAGGTGAAAGATGTCATTCAATACGTTG
ATTATTTCCATGCAATTGGACTCAGTAAAGCTAGCAGGGGAAATTCAAAAAAGAAAGTGACCGAGTCA
AGTGTCTTCTTCAAGTAAATATTTCTAAAGAAGAAAGCAAACACGGTTTTTCGAGAGAGGAACTGCTGGA
AATCTTGCCAGAGTTAGCCAGACTAGATAAGATTGAATATGTTGGTTTAAATGACGATGGCACCTTTTGA
GCTAGCAGTGACAGTTGAAAGAGATTTTCAAGGCGGCCCAAGATTACAAAGAGAAATTCAAGAGAAA
CAAATTCCAAATATGCCTATGACCGAGTTAAGTATGGGAATGAGTCGTGATTATAAAGAAGCGATTCAAT
TCGTTTCACTTTTGTTCGTATAGGTACATCATTTTTAAGTAG

2 CFE15 "homologue of SEQ. ID NO. 15"

ATGGGAATTGCTCTAGAAAATGTGAATTTTATATATCAAGAAGGTACTCCCTTAGCTTCAGCAGCTTTGTC
GGATGTTTCTTTGACGATTGAAGATGGCTCTTATACAGCTTTAATTGGGCACACAGGTAGTGGTAAATCA
ACTATTTTACAACCTCTTAAATGGTTTATTGGTGCCAAGTCAAGGGGAGTGTGAGGGTFTTTGATACCTTAAT
CACCTGACTTCTAAAAATAAAGATATTCGTCAAATTAGAAAACAGGTTGGCTTGGTATTTCACTTTGCT
GAAAATCAGATTTTGAAGAAACGGTTTGAAGGACGTTGCTTTTGGACCGCAAAATTTGGAGTTTCTG
AAGAAGATGCTGTGAAGACTGCGCGTGAGAACTGGCTCTGGTTGGAATTGATGAATCACTTTTGTATCG
TAGTCCGTTTGAAGCTGTGAGGGGGACAAATGAGACGTGTTGCCATTGCAGGCATCTTGGCATGGAGCCA
TGTATATTAGTCTTAGATGAGCCAACAGCTGGTCTAGATCCTCTAGGGAGAAAAGAGTTGATGACCCTGT
TCAAAA AACTCCACCAGTCAGGGATGACCATCGTCTTGGTAACGCATTTGATGGATGATGTTGCTGAATA
TGCTAATCAAOTCTATGTAATGGAAAAGGGACGTTTAGTAAAGGGGGGCAACCAAGTGATGCTTTCA
AGACGTGTTTATGGAAGAAGTTCACTTGGGAGTACGTAAAATTACGGCCTTTTGTAAACGATTGGCT
GATAGAGGCGTGTCAATTAAACGATTACCGATTAAGATAGAGGAGTTCAAGGATCGCTAAATGGATAG

2 CFE16 "homologue of SEQ. ID NO. 16"

ATGGATATTCAATTTTATAGGAACGGGGGCTGGTTCAGCCCTCTAAAGCCCGCAACGTTTCAAGTCTCGCCC
TGAAACTCTTGGATGAGATTAACGAAGTTTGGCTCTTTGACTGTGGAGAAGGTACGCAAAATCGCATTCT
GCAAAACCAATTCGACCACGTAAGGTGAGCAAAATCTTTATTACCCATCTGCATGGAGACCACATTTT
GGTTTCCAGGTTTCTTCTAGCCGTGCTTTTCAAGGCCAATGAAGAGCAGACAGATTTGGAAATCTACG
GACCTCAAGGAATCAAGTCATTTGTCTTAACCAGCCTTCGTGTGTGTCAGGTTCTCGTCTGCCCTACCGCATT
CATTTCCATGAGTTTGACCAAGATTCTCTGGGTAAAATTCTTGAAACCGATAAAATTCAGTGTGTATGCAGA
GGAGCTGGACCACACTATTTTCTGTGTTGGCTATCGTGTGTCATGCAAAAGGATCTAGAAGGGACGCTGGAT
GCTGAAA AACTCAAGGCTGCTGGTGTTCGGTTCCGGCCCGCTTTTGGTAAAATCAAAAACGGCCAGGATC
TTGTTTGGAAAGACGGAAGTGAATCAAGGCAGCAGACTATATCTCAGCGCCACGTCACAGGTAAGATTAT
CACTATTTTAGGAGACACTCGAAAACGGGTGCCAGTGTGCGTCTGGCTGTCAATGCAGATGTCCTAGTT
CATGAGTCCACTTATGGCAAGGGTGATGAAAAAATTGCTCGTAACCATGGTCACTCACTAATATGCAAG
CTGCAGAGTAGCGGTAGAAGCAGGTGCCAAACGCCCTCTACTCAACCATATCAGTGCCCGTTTCTCTC
AAAAGATATTAGCAA AACTCAAGAAAGACGCTGCCACAATTTTGA AAAATGTCCATGTGGTCAAAGACTTG
GAAGAAGTGGAATCTAG

2 CFE17 "homologue of SEQ. ID NO. 17"

ATGAGTAAATCAGTTTAAACAACACTTGGTGGTGTGCGTGAGAATGGAAAAAATATGTACATTGCTGAAA
TTGGAGAGTCCATTTTGTTTTGAATGTAGGGTTAAAATATCCTGAAAATGAACAATTAGGGGTGCGATGT
GGTGATTCCAAACATGGATTACCTTTTGA AAAATAGCGACCGTATTGCTGGGGTFTTCTTGACCCACGGGC
ATGCGGATGCCATTGGTGCTCTACCTTATCTCTTGGCAGAGGCTAAAGTTCTGTATTGGGTCTGAGTTG
ACCATTCAGTTGGCAAAGCTCTTTGTCAAAGGAAATGATGCCGTTAAGAAATTTAATGATTTCATGTCA
TTGATGAGAATACGGAGATTGATTTTGGTGGGACAGTGGTTTCTTCTTCCCTACGACTTACTCCGTTCCA
GAGAGTCTGGGAATTGTCTTGAAGACATCGGAAGGAAGCATCGTTTATACAGGTGACTTCAAATTTGACC
AAACGGCTAGTGAATCTTATGCAACTGATTTTGTCTGTTTGGCAGAGATTGGTCTGTGACGGCGTCTGGC
TCTCTCAGTGATTCCGGCCAATGCAGACAGCAATATTAGGTGGCTAGTGAAAGTGAAGTTAGGGATGAA
ATTAGCCAAACTATTGCTGACTGGGAAGGTCTGATCATCGTTGACAGCTGTTTCCAGTAATCTTCTCGTAT
TGAGCAGATTTTGGACGCTGCGGATAAAACAGGTGACGATCGTCTTGACAGGATTGATATTGAAAAT
ATGCTCCCAACAGCGATTCTGTCTTAAGAAGTTGTCTTTAGCCAACGAAATTTCTCTTGATTAAAGCCTAAAG
ATA TGTCTCGCTTTGAAGACCATGAGTTGATTATTCTTGAGACAGGTCTGATGGGTGAACCTATCAATGG
AGTTCGTAAAGATGTCGATTGGTCTGCCATCGTTATGTAGAAATCAAGGATGGGGACCTGGTCTATATTGCT
ACCGCTCCGTCTATTGCTAAAGAAGCCTTTGTTGCGCGTGTGGAAAATATGATTTATCAGGCAGGTGGGG
TTGTGAAATTGATTACCCAAAGTTTACATGTATCAGGGCACGGAAATGTGCGTGATTGTCAGCTGATGAT
CAATCTTTTGCAACCTAAGTACCTCTTCCCTGTCCAAGGGGAGTATCGTGAGTTGGATGCTCACGCTAAG
GCTGCGCATGGCAGTTGGGATGTTGCCAGAACGCATCTTCACTCTAA AAGGGGACGACCATGGCTTACG
AGAATGGAGACTTGTTCAGCTGGATCGGTTTCAAGCAGGAGATATCTTGATTGATGGGAATGCCATTGG
TGATGTTGGAAATGTTGTTCTTCTGTGACCGTAAGGTCTTGTGACAGGATGGAATTTTCACTCGTGGCTATTA
CAGTCAACCGTCTGTGAGAAGAAATTGTGGCTAGAGCTCGTGTTCACACGCGTGGATTGTTTATCTCAA
GAAGAGTCCGATATTCTCCGTGAAAGTTTCAAGATTGATTAACCAACGGTAGAAGAGTATCTTCAAGG
AGATGACTTTGACTGGGCAGATCTCAAAGGTAAGGTTCTGTGACAATCTGACCAAGTACCTCTTGATCAA
ACCAAGGTCGCCAGCCATTTTACCAGTAGTCATGGAAGCAAAATAA

2 (CFE19) "homologue of SEQ. ID NO. 18"

ATGACAAAAGAATTTTCATCATGTAAACGGTCTTACTCCACGAAACGATTGATATGCTTGACGTAAAGCCTG
AAGGTATCTACGTTGATGCGACTTTGGGCGGAGCAGGACATAGCGAGTATTTATTAAGTAAATTAAGTGA
AAAAGGCCATCTCTATGCCTTTGACCAGGATCAGAATGCCATTGACAATGCGCAAAAACGCTTGGCACCT
TACATTBAGAAGGGAATGGTGACCTTTATCAAGGATAACTTCCGTCAATTACAGGCACGTTTGGCGGAAG
CTGGTGTTTCAGGAAATTGATGGAATTTGTTATGACTTGGGAGTGTCTAGTCCCTCAATTGGACCAGCGTGA
GCGTGTTTTTCTTATAAAAAGGATGCGCCACTGGACATGCGGATGAATCAGGATGCTAGTCTGACAGCC
TATGAAGTGGTTAATCATTATGACTATCATGATTTGOTTCGTATTTTCTTCAAATACGGTGAGGATAAATT
CTCTAAACAGATTGCGCGTAAGATTGAGCAAGCGCGTGAAGTGAAGCCGATTGAGACAACGACTGAGTT
AGCAGAGATTATCAAGTTGGTCAAACCTGCCAAGGAACCTCAAGAAGAAGGGTCACTCTGCTAAGCAGAT
TTCCAGGCTATTGCAATTGAAGTCAATGATGAACTGGGAGCGGCAGATGAGTCCATCCAGCAGGCTATG
GATATGTTGGCTCTGGATGGTAGAATTTCAAGTATTACCTTTTATTCTTAGAAGACCGCTTGACCAAGCA
ATTGTTCAAGGAAGCTTCAACAGTTGAAGTTCCAAAAGGCTTGCCTTTTATCCAGATGATCTCAAGCCC
AAGATGGAATTGGTGTCCCGTAAGCCAATCTTGCCAAGTGCGGAAGAGTTAGAAGCCAATAACCGCTCG
CACTCAGCCAAGTTGCGCGTGGTCAGAAAAATTCAAGCTCGAGCACCACCACCACCACCACTGA

2 CFE21 "homologue of SEQ. ID NO. 19"

ATGAGTAGAATTTTAGATAATGAGATAATGGGGGATGAGGAGTTAGTAGAACGCACGCTCCGTCCTCAG
TATTTACGTGAATATATCGGACAGGATAAGGTCAAGGACCAGGTACAAATCTTTATTGAAGCTGCCAAAA
TGCGGGATGAAGCGCTGGATCATGTGCTCTTATTTGGGCGCTCCAGGTCTCGGGGAAAACGACCATGGCCTT
TGTTATTGCCAACGAACCTGGGAGTCAATCTTAAGCAGACGTCGGGTCCAGTCAATTGAAAAAGCCGGAGAT
CTGGTAGCTATTTTGAATGAGTTAGAGCCTGGGGATGTCTTTTTATTGATGAGATCCATCGTTTGCCAAT
GTCACTGGAAGAGGTGCTTTATAGTGCTATGGAGGACTTCTACATAGATATTATGATTGGGGCTGGTGAG
GGTAGTGTAGTGTTCATTGAGGTTACCACCTTTTACCTTGATTGGTGCGACGACTCGGGCTGGTATGCT
CTCCAATCCGCTACGGGCACGTTTTTGGGATTACAGGCCATATGGAGTATTATGCCCATGCTGACTTGACA
GAAATTGTCGAGCGGACGGCAGATATTTTGAAGATGGAAATCACTCATGAGGCAGCATCTGAGTTGGCCC
TACGTATCGTGGGACCCCTCGTATTGCCAATCGTCTCGTCAAGCGCGTGCGCGATTTTGCCCAAGATAATG
GGGAATGGGGTAATTGATGATATTATTACCGATAAGGCTTTGACTATGCTGGATGTTGACCATGAAGGTT
TGGACTATGTGGATCAAAAAATCCTTCGTACCATGATTGAGATGTACAGTGGAGGACCTGTTGGTCTAGG
AACTCTTTCTGTGAATATCGCCGAAGAGCGTGAGACAGTTGAAGACATGTATGAGCCTTACTTGATTCAA
AAAGGTTTATCATGCGGACACGGTCTGGACGGGTGGCGACTGCTAAGGCATATGAGCACTTAGGTTATG
AATACATGAAAAAGCGGCGCACTCGAGCACCACCAGCACCACCACCTGA

2 CFE24 "homologue of SEQ. ID NO. 20"

ATCAGTATGTTTTAGATACAGCTAAGATTAAGGTCAAGGCTGGTAATGGTGGCGATGGTATGOTTGCCCT
TTGGTGGTGAAAAATATGTCCCTAATGGAGGCCCTTGGGGTGGTGATGGTGGTGGTGAGGCAATGTGGT
CTTCGTTGTAGACGAAGGACTACGTACCTTGATGGATTTCGGCTACAATCGTCAATTTCAGGGCTGATTCTG
GTCAAAAAGGGATGACCAAGGGATGCATGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGT
GTACGACTGTTCTGTATGCGGAGACTGGCAAGGTTTTAACAGATTGATTGAACATGGGCAAGAATTTAT
CGTTGCCACCGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGT
ATCTCTGAAAAATGGAGAACCAGGTCAGGAACGTGAGTTACAATTGGAACATAAAAAATCTTGGCAGATGTC
GGTTTAATAGGATTCCTCATCTGTAGGGGAAGTCAACACTTTTAAGTGTTATTACCTCAGCTAAGCCTAAAAAT
TGGTGGCTACCACTTTACCACTATTGTACCAAAATTTAGGATGGTTTCGCACCCAATCAGGTGAATCCTTTG
CAGTAGCCGACTTGCCAGGTTTGATTGAAGGGGCTAGTCAAGGTGTTGGTTTGGGAAGTCAAGTTCCCTCCG
TCACATCGAGCGTACACGTGTTATCCTTCACATCATTGATATGTCAGCTAGCGAAGCCCGTGATCCATATG
AGGATTACCTAGCTATCAATAAAGAGCTGGAGTCTTACAATCTTGGCCTCATGGAGCGTCCACAGATTAT
TGTAACATAAAGATGGACATGCCTGAGAGTCAGGAAAATCTTGAAGAATTTAAGAAAAAATTGGCTGA
AAATTATGATGAATTGGAAGAGTTACCAGCTATCTTCCCAATTTCTGGATTGACCAAGCAAGGTCTGGCA
ACACTTTTAGATGCTACAGCTGAATTGTTAGACAAGACACCAGAATTTTGGTCTACGACGAGTCCGATA
TGGAGAAGAAGTTTACTATGGAATTGACGAAGAAGAAAAAGCCTTTGAAATTAAGTCGTGATGACGATG
CGACATGGGTACTTTCTGGTGAAAACTCATGAACTCTTTAATATGACCAACTTTGATCGTGATGAATCT
GTCATGAAATTTGCCCGTCAGCTTCGTGGTATGGGGGTTGATGAAGCCCTTCGTGCGCGTGGAGCTAAAG
ATGGGGAATTTGGTCCGCAATTGGTAAATTTGAGTTTGAATTTGATGACCTCGAGCACCACCACCACCAC

18a

2 CFE25 "homologue of SEQ. ID NO. 21"

ATGAAC TACTTTAATGTTGGGAAAATCGTTAATACGCAGGGATTACAGGGTGAGATGCCAGTCTTGTCTG
TGACGGATTTTGCAGAAGAACGGTTTAAAAAAGGAGCTGAGCTGGCTTTGTTTGATGAAAAAGATCAGTT
TGTCCAAACAGTGACCATCGCTAGCCACCGTAAACAGAAGAACTTTGACATTATTAATTCAAAGATATG
TACCATATCAATACTATCGAAAAGTACAAGGGGATACAGTCTCAAGGTCGCTGAGGAAGATTGGAATGAC
CTAGACGATGGTGAAATTTACTATCACGAGATTATCGGTTTGGAAAGTCTATGAGGGTGATAGCTTGGTTG
GAACCATCAAGGAAATCCTGCAACCAGGTGCTAATGATGTCTGGGTGGTCAAACGAAAAGGCCAAACGTG
ATTGGCTTTTACCTTATATCCACCAAGTGGTTCTCAATGTTGATATTCCAAATAAACGGGTGATGTGGAA
ATCTTAGAAGGGTTAGACGATGAAGATCTCGAGCACCACCACCACCACCACTGA

2 CFE26 "homologue of SEQ. ID NO. 22"

ATGAAGATTGATATTTTAACCTCTTTCCAGAGATGTTTTCTCCACTGGAGCACTCAATCGTTGGAAAGGC
TCGAGAAAAAGGGCTCTTGGATATCCAGTATCATAATTTTCGAGAAAAATGCTGAAAAGGCCCGTCATGTA
GATGATGAGCCCTACGGAGGCGGTGAGGGCATGTTGCTCAGAGTACAACCTATTTTCGATTCTCTTGATG
CTATTGAAAAAAGAAAAATCCGCGCGTTATTCTCTCGATCCTGCTGGAAAGCAAGTTTGTATCAGGCTTATGC
TGAAGATTGGCTCAAGAGGAAGAGCTAATCTTTATCTGTGGGCACTATGAGGGTTATGATGAGCGCATT
AAGACCTTGGTAACAGATGAGATTTCCTAGGCGACTATGTTCTCACTGGTGGAGAATTGGCAGCTATGA
CCATGATTGATGCTACAGTTCCGCTGATTCCAGAAGTGATTGGCAAGGAGTCTAGCCACCAAGATGATAG
TTTTCTTCAGGCTTTTTAGAAATATCCTCAGTACACACGTCCTATGATTATCGAGGCATGGTCGTGCCAG
ATGATTTGATGAGTGGTCACCATGAAAAGATTCTGTCAGTGGCGATTGTACGAGAGTTTAAAGAAAACCTA
CGAGCGCAGGCCGGATTTACTTGAACATTATCAACTGACAGTAGAAGAAGAAAAAATGCTGGCAGAAAT
CAAAGAAAACAAAGAAGCGGCCGCACTCGAGCACCACCACCACCACCACTGA

2 CFE27 "homologue of SEQ. ID NO. 23"

ATGATTCAAGCAAGTAAATTAAGCTGGTATGACCTTTGAAACAGCTGACGGCAAATTGATTCCGCGTTT
TGGAAGCTAGTCACCACAAACCAGGTAAAGGAAACACGATCATGCGTATGAAATTGCGTGATGTCCGTA
CTGGTTCTACATTTGACACAAGCTACCGTCCAGAGGAAAAATTTGAACAAGCTATTATCGAGACTGTCCC
AGCTCAATACTTGTACAAAATGGATGACACAGCATACTTCATGAATACAGAACTTATGACCAATACGAA
ATCCCTCTAGTCAATGTTGAAAACGAATTGCTTTACATCCTTGAAAACCTCTGATGTGAAAATCCAATTCTA
CGGAAC TGAAAGTATCGGTGTCACCGTTCTACTACTGTTGAGTTGACAGTTGCTGAAAACCTCAACCATCT
ATCAAAAGGTGCTACTGTTACAGGTTCTGGTAAACCAGCAACGATGGAAACTGGACTTGTCTGTAACGTTT
CAGACTTCATCGAAGCAGGACAAAAACTCGTTATCAACACTGCAGAAGGAACCTTACGTTTCTCGTGCCCT
CGAGCACCACCACCACCACCACTGA

2 CFE28 "homologue of SEQ. ID NO. 24"

ATGGCATTGAAAATTTAACAGAACGTTTGCAGAACGTCTTTAAAAATCTACGTAAAAAAGGAAAAATCT
CTCAATCTGATGTCCAAGAGGCAACCAAGAAATTCGCTTGGCCTTGCTCGAGGCCGACGTTGCCCTTGGC
TGTTGTAAAGGACTTTATCAAGAAAGTTAGTGAGCGTGACGTCGGGCATGAGGTCAATTGATACACTTAAT
CCTGGCGAACAGATTATTAATAATCGTTGATGAGGAACTGACAGCCGTTTTAGGTTCTGATACGGCAGAAA
TTATCAAGTCACTAAGATTCCAACCATCATCATGATGGTTGGTTTACAAGGGGCTGGTAAACAACCTT
TGCTGGTAAATTTGGCCAACAACCTCAAGAAAGAAGAAAAATGCTCGTCCTTTGATGGTTGCGGCGGATATT
TATCGTCCAGCTGCCATTGACCAGCTTAAGACCTTGGGACAACAGATTGATGTGCCTGTCTTTGCACCTTG
AACAGAAAGTACAGCTGTTGAGATTGTACGTCAAGGTTTGGAGCAAGCCCAACTAATCATAACGACTAT
GTCTTCAATTGATACTGCGGGTCTGTTTGCAGATTGATGAGCTCCTCATGAATGAGCTTCGTGATGTGAAAG
CATTGGCTCAACCAATGAAATCTTGGCTTGTCTGTTGATGCTATGATTGGTCAGGAAGCAGCCAATGTTGC
GCCTGAGTTTAATGCTCAGTTGGAAGTGAAGTGGGGTCACTCCTTACCAAGATTGATGGCGATACTCGTGGT
GGTCTGCTCTGTCTGTTCTGTCACATTACTGGAAAACCAATCAAGTTCACCTGGTACAGGTGAAAAGATTA
CGGAATTGAAAACCTTCCACCCAGACCGCATGTCTAGCCGTATCCTTGGTATGGGGGATATGCTCACTTT
GATTGAGAAAGCTTCTCAGGAATACGATGAACAAAAAGCCCTTGAAATGGCTGAGAAGATGCGCGAAAA
CACCTTTGATTTAATGATTTTCATCGATCAATTAGATCAGGTGCAAAATATGGGGCCGATGGAAGACTTG
CTCAAGATGATTCAGGTATGGCCAACAATCCAGCCCTTCAAAACATGAAGGTGGATGAACGCCAGATT
GCTCGTAACGTTGCCATTGTGTCTTCGATGACACCTGAAGAGCGTGAAAACCCAGATTTGTTAAATCCAA
GCCGTGCGCGTGTGATTGCTGCTGGTTCTGGAAATACATTCTGTCGAAGTCAATAAATTCATCAAGGACTTT
AACCAGGCTAAACAGCTCATGCAGGGTGTATGTCTGGGGATATGAATAAAATGATGAAGCAAAATGGGG
ATTAATCCAAATAACCTTCTTAAAAATATGCCAAATATGGGAGGAATGGATATGTCTGCCCTTGAAGGAA

2 CFE 28 (contd)

(Contd.)
Fig 49
TCATGGGACAAGGCGGTATGCCTGACTTATCAGCTCTCGGAGGAGCAGGAATGCCAGATATGAGCCAGA
TGTTCGTGGCGGTTTGAAAGGTAAAATTGGTGAATTTGCCATGAAACAGTCCATGAAACGTATGGCTAA
CAAAATGAAGAAAGCGAAGAAGAAACGCAAGGCGGCCGCACTCGAGCACCACCACCACCACCTGA

2 CFE29 "homologue of SEQ. ID NO. 25"

Fig 50
ATGATCTTATTGAAATTTTAAAATCTATCTTCTTCGGGATTGTTGAAGGAATTACGGAATGGTTGCCGAT
TTCCAGTACAGGTCACCTTGATTTTAGCAGAGGAGTTTATCCAATACCAAAATCAAAATGAAGCCTTTATG
TCCATGTTTAATGTCGTGATTACAGCTTGGTGCTATTTTAGCAGTTATGGTGATTTATTTTAACAAGCTCAAT
CCTTTTAAAOCCGACTAAGGACAAACAGGAAGTTTCGTAAAGACTTGGAGACTATGGTTGAAGGTCTTGATTG
CCACTTTGCCCTTACTTGGTGCTTTTAAATTTGATGATTGGTTTGATACCCACTTCCATAACATGGTTTCAG
TTGCTGTCATGTTGATTATCTACGGGGTTGCCTTCATCTATTTGGAAAAGCGCAATAAAGCGCGTGCTATC
GAGCCAAGTGTAACAGAGTTGGACAAGCTTCCTTATACGACCGCTTCTATATCGGACTCTTCCAAGTTCT
TGCTCTTTTACCAGGGACTAGCCGTTACGGTGCAACGATTGTGCGGTGGTTTGTTAAATGGAACCAAGTCGTT
CAGTTGTGACAGAATTTACCTTCTATCTTGGGATTCCCGTTATGTTTGGAGCTAGTGCCCTTAAAGATTTTC
AAATTGTGAAAGCCGGAGAAGCTTTGAGCTTTGGGCAATTGTTTTGCTCTTGGTTCGCGATGGGAGTAG
CTTTTGGCGTCAGCATGGTGCTATTGCTTCTTGACCAGCTATGTGAAAAACACGACTTCACCCTTTT
GGTAAATACGGTATCGTGCTTGGTAGTGTTTGTCTACTTTACAGTTTGTCCGTTTATTTGTACTCGAGCAC
CACCACCACCACCTGA

2 CFE30 "homologue of SEQ. ID NO. 26"

Fig 51
ATGGGATTATTTGACCGTCTATTCGGAAAAAAGAAGAACCTAAAATCGAAGAAGTTGTAAAAGAAGCT
CTGGAAAAATCTTGATTGTCTGAAGATGTTGATCCTACCTTCACAGAAGTTGAGGAAGTTTCTCAGGAAG
AAGCAGAGGTTGAAATTGTTGAACAAGCTGTGTTCCAAGAAGAGGAAATCCAAGACACAGTTGAAGAAA
GTCTGGATTTAGAGCCAGTTGTAGAAGTTTCTCAAAAAGAAGTCGAAGAATTTCCCACTCAGAAGAAGG
GAATACTGAGTTTCTAGAGACTATAGAAGAAAATAATTCTGAAGTTCTTGAACCAAGAAAGGCCTCAAGC
AGAAGAAACCGTTACAGGAAAAATATGACCGCAGTCTTAAGAAAACCTCGTACAGGTTTCCGGTGCCCGCTT
GAATGCTTCTTTGCTAACTTCCGCTCTGTGACGAAGAATTTTTCGAGGAAGTGAAGAAGTCTGATTGA
TGAGTGATGTTGGTGTCGAAGTCGCTTCTAACTTAACGGAGGAAGTACGTTACGAAGCCAAGCTTGAAAA
TGCCAAGAAACCTGATGCACTTCGTGCTGTCATCATTGAGAAATTGGTTGAGCTTTATGAAAAGGATGGT
AGCTACGATGAAAGCATCCACTTCCAAGATAACTTGACAGTTATGCTCTTTGTTGGTGTAATGGTGTTG
GGAAAAACAACCTTCTATCGGAAAACTAGCCACCGCTACAAACAAGCTGGTAAGAAGGTCATGCTGGTTG
CAGCAGATACCTTCCGTGCGGGTGCACTAGCTCAGCTAGCTGAATGGGGCCGACGAGTAGATGTTCCAGT
AGTAACTGGACCTGAAAAAGCTGATCCAGCCAGCGTGGTCTTTGATGGTATGGAACGTGCCGTGGCTGAA
GGTATCGATATTCTCATGATTGATACTGCTGGTCTGCAAAATAAGGATAACCTTATGGCTGAGTTGG
AAAAGATTGGTCTGATTATCAAACGTGTTGTGCCAGAAGCACCACATGAAACCTTCTGGCACTTGATGCA
TCAACAGGTCAAATGCCCTAGTACAGGCCAAAGAATTTTCGAAAAATCACACCTTTAACGGGAATTGTTT
TGACTAAGATTGATGGAAGTCTCGAGGAGGTGTGGTTCTAGCCATTCTGTGAAGAACTCAATATTCCTGT
AAAAATTGATTGGTTTTGGTGAAAAAATCGATGATATTGGAGAGTTTAACTCAGAAAACTTTATGAAAGGT
CTCTTGCAAGGTTTAATCGCGGCCGCACTCGAGCACCACCACCACCACCTGA

2 CFE31 "homologue of SEQ. ID NO. 27"

Fig 52
ATGTATATTGAAATGGTAGATGAAACTGGTCAAGTTTCAAAAAGAAATGTTGCAACAAACCCAAGAAATTT
TGGAATTTGCAGCCCAAAAATTAGGAAAAGAAGACAAGGAGATGGCAGTCACTTTTGTGACCAATGAGC
GTAGTCATGAACCTAATCTGGAGTACCGTGACACCGACCGTCCGACAGATGTCATCAGCCTTGAGTATAA
ACCAGAATTGGAATTTGCCCTTTGACGAAGAGGATTGCTTGAAAATCCAGAAATGGCAGAGATGATGCT
GAGTTTGATGCCTATATTGGGGAAATTGTTTCTCTATCGATAAGGCTCATGAGCAGGCCGAAGAATATG
GTACAGCTTTGAGCGTGAGATGGGCTTCTTGGCAGTACACGGCTTTTACATATTAACGGCTATGATCAC
TATACTCCGGAAGAAGAGCGGAGATGTTCCGGTTTACAAGAAGAAATTTTGACAGCCTATGGACTCACA
AGACAACTCGAGCACCACCACCACCACCTGA

2 CFE32 "homologue of SEQ. ID NO. 28"

Fig 53
ATGAGTATTCGAGTAATTATTGCCGGTTTAAAGGGAAAGATGGGCCAGGCTGCTTGTGAGATGGTATTGA
CTGATCCAGACTTGGACTTGGTGGCAGTTTGGATCCTTTTGAATCTGAGTCAGAATGGCAGGGTATTCCT
GTTTTCAAGGATAAGGCTGATTAGCTGGTTTTGAAGCGGATGTCTGGGTAGATTTTACTACTCCAGCTGT
TGCCTACGAAAATACACGTTTTGCTCTTGAAAATGGCTTTGCTCCAGTAGTTGGAACGACTGGTTTCACGA

2CFE 32

GTGAAGAAATTGCAGAGCTAAAAGAATTTTCTCGTGCCCAAGACTTGGGTGGCCTGATTGCCCTAACTT
TCCCTIGGGTGCTGTCTTACTCATGCAATTTGCCGACGCAGGCTGCCAAATATTTCCCAAATGTGGAGATTA
TTGAGCTCCATCATGACAAGAAAAGGATGCTCCGAGTGGAAACAGCCATTAAAACAGCTGAGTTGATGG
CAGAGGTTTCGAGAGTCCATTACAGCAAGGCGCAGCAGATGAGGAAGAGCTGATTGCTGGTGGCTCGTGGTG
CTGACTTTGATGGTATGCGCATCCACTCAGTTTCGTTTGCCAGGCTTGGTAGCTCATCAAGAAGTCATCTTT
GCCAATCAGGGAGAAGGGTTGACCCCTCCGTCATGACTCCTATGATCGCATCTCCTTCATGACAGGAGTCA
ATTTGGGAATTAAGAAGTTGTCAAGCGTCATGAGCTTGTCTATGGATTAGAACACTTATTACTCGAGCA
CCACCACCACCACCTGA

2CFE33: "homologue of SEQ. ID NO. 29"

ATGGCAAAACAAACAAGATTTGATCGCTAAAGTAGCAGAAGCTACAGAATTGACTAAGAAAGACTCAGCA
GCAGCAGTTGAAGCTGTATTTGCAGCAGTAGCTGACTATCTTGCAGCTGGTGAAAAAGTTCAATTGATCG
GTTTTGGTAACTTTGAAGTTTCGTGAGCGTGCGAAGCGTAAAGGTCGCAACCCACAACTGGTAAAGAAAT
GACAAATGCAAGCTTCTAAAGTACCAGCATTCAAAGCTGGTAAAGCTCTTAAAGACGCTGTAAACTCGAG
CACCACACCACCACCTGA

2CFE34: "homologue of SEQ. ID NO. 30"

ATGACTAAAACAGCCTTTTTTATTGCTGGTCAAGGTGCCCAGTATCTAGGGATGGGACGGGATTTCTATG
ATCAGTATCCGATTGTTAAAGAAACGATTGATCGAGCGAGTCAGGTGCTAGGTTATGATTGCGTTATCT
CATCGATACGGAAGAAGACAACTCAATCAGACCCGCTATACGCAACCAGCCATTCTAGCGACTTCGGTT
GCTATCTACCGTTTATTGCAAGAAAAGGGCTATCAGCCTGATATGGTTGCTGGTTTGTCTCTTGGAGAATA
CTCTGCCCTTGGTGGCAAGCGGCGCCTTGGATTTTGAAGATGCGGTTGCTTGGTAGCTAAGCGTGGAGGC
TATATGDAAGAAGCGGCTCCTGCTGACTCTGGCAAGATGGTAGCAGTTCTCAATACGCCAGTAGAGGTCA
TTGAAGAAGCCTGTCAAAAAGCTTCTGAAGTTGGAGTGGTTACTCCAGCCAACCTATAACACACCTGCACA
AATCGTCATTGCTGGAGAAGTGGTTGCAGTTGATCGAGCGGTTGAACCTTTTGAAGAAGCAGGTGCCAAA
CGCTTGATTCTCTTAAAGGTGTCAGGTCCCTTTTCAACCTCTCTCCTTGAACCTGCTAGCCAGAACTAGC
TGAAAGCTCTGGCTCAGGTAAGTTTTTTCAGATTTTACTTGTCCCTAGTCGGCAATACAGAAGCTGCTGTGA
TGCAAAAAGAGGACATTGCTCAGCTCTTACGCGTCAGGTCAAGGAACCCGTTTCGTTTCTATGAAAGTAT
TGGGGTCATGGAAGAAGCAGGCATAAGCAACTTATCGAGATTGGACCGGGGAAAGTCTTGTGAGGTTT
GTTAAAAAAATTGATCAAACTGCTCACTTAGCTCATGTGAAGATCAAGCGAGTTTAGTAGCACTTTTAG
AAAAACTCGAGCACCACCACCACCACCTGA

2CFE35: "homologue of SEQ. ID NO. 31" 35

ATCAAACTAGAACATAAAAATATCTTTATTACAGGTTTCGAGTCTGGAATTGGTCTTGCCATCGCCCAQA
AGTTTGCTCAAGCAGGAGCCAACATTGTCTTAAACAGTCTGGGGCAATCTCAGAAGAAATTGCTGGCTGA
GTTTTCAAACTATGGTATCAAGGTGGTTCCCAATTCAGGAGATGTATCAGATTTTGCAGACGCTAAGCGT
ATGATTGATCAAGCTATTGCAGAAGTGGGTTTCAGTAGATGTTTGGTCAACAATGCAAGGATTACCCAAG
ATACTCTTATGCTCAAGATGACAGAAGCAGATTTTGAAAAAGTCTCAAGGTCAATCTGACTGGTGGCTT
TAATATCACAATCAGTCTTGAACCGATGATGAAGCCAGAGAAGGTGCTATCATTAAATATGTCTAGT
GTGTGTTGGTTTGTATGGGGAATATTGGTCAAGCTAACTATGCTGCTTCTAAGGCTGGCTTGTATGGCTTAC
CAAGTCTGTGGCACGCGAGGTTCGCTAGTCGGAATATACGAGTCAATGTGATTGCTCCAGGAATGATTGAG
TCTGATATGACAGCTATCTTATCAGATAAGATTAAAGGAAGCTACACTAGCTCAGATTCCGATGAAAGAAT
TTGGGCAGGCAGAGCAGGTTCAGATTGACAGTATTTTAGCAGGGCAAGATTATCTAACTGGTCAAGT
GATIGCCATTGATGGTGGCTTAAGTATGCTCGAGCACCACCACCACCACCTGA

2CFE36: "homologue of SEQ. ID NO. 32"

ATGGGAGTGAAAAAGAACTAAAGTTGACTAGTTTGCTAGGACTGTCTCTGTTAATCATGACAGCCTGTG
CGACTAATGGGGTAACTAGCGATATTACAGCCGAATCGGCTGATTTTGGAGTAAATTGGTTTACTTCTTT
GCGGAAATCAATTCGCTTTTTATCGTTTGATATTAGTATCGGAGTGGGGATTATCTCTTTACGGTCTTGAAT
CGTACAGTCTCTTGGCAGTCTTTCAGGTGCAAAATGGTGGCTTCTAGGAAAATGCAGGAAGCTCAGCCAC
GCATTAAAGGCGCTTCGAGAACAAATATCCAGGTTCGAGATATGGAAAGCAGAACCAAACTAGAGCAGGAAA
TGCGTAAAGTATTAAAGAAATGGGTGTCAGACAGTCAAGTCTCTTGGCCGATTTTGATTTCAGATGGC
GGTTATTTTGGCCCTGTTCCAAGCCCTATCAAGAGTTGACTTTTAAAGACAGGTCAATTCCTTATGGATTA
ACCTTGGTAGTGTGGATACAACCCTTGTCTTCCGATTTTAGCAGCAGTATTCACCTTTTAAAGTACTTGG
TTGTCCAACAAAGCTTTGTCTGAGCGAAATGGCGCTACGACTGCGATGATGTATGGGATTCCAGTCTTGA
TTTTATCTTTCAGTTTATGCGCCAGGTGGAGTCGCCCTATACTGGACAGTGTCTAATGCTTATCAAGTC

2 CFE 36

(cont'd) Fig 57
TTGCAAACCTATTTCTTGAATAATCCATTCAAGATTATCGCAGAGCGCGAGGCCGTAGTACAGGCACAAA
AAGATTTGGAAAATAGAAAAAGAAAAGCCAAGAAAAAGGCTCAGAAAACGAAACTCGAGCACCACCAC
CACCACCACTGA

2 CFE37 "homologue of SEQ. ID NO. 33"

Fig 58
ATGAAGATTAGTAAGAGGCACTTATTAAATTATTCATCTTGATTCCCTACTTGCTTTTATCTATTTTGGGC
TTGATTGTGGTCTATTTCGACCACCAGTGCTATTTTAATTGAAGAAGGCAAGAGCGCCTTGCAAGTTGGTTCG
AAACCAAGGAATCTTTTGGATTGGTAGTTTGATACTGATTGCCTTAATTTATAAATTGAGACTAGATTTTT
TGAGAAATGAGCGACTAATCATTTTAGTTATATTAATAGAAATGCTTTTATTGTTCTTGGCTCGTTTTATT
GGTATTTCAGTAAACGGGGGCATACGGTTGGATTTCGGTTGCAGGAGTAACCTATTCAGCCAGCTGAGTACT
TAAAAATCATTATTATTTGGTATTTAGCTCACCAGATTCTCCAAACAGCAAGAAGAAATAGCTACTTATGA
TTTTCAAGTTTGTACTCAAAATCAATGGCTTCCCCGTGCTTTTAATGATTGGCGATTCTGTTCTCCTAGTTCT
GATTGGAAGTTTGGGAATTTTCCCTGATTTAGGAAATGCGACTATTTTAGTCTTGGTTTCTTGATTATGT
ATACAGTTAGTGGAATCGCTTATCGCTGGTTTTCAACCATTCCTGGCGCTCGTATCTGCGCGCTTCTGTCTTTG
TCTTGACCACTATCAGCCTAATCGGTGTTGAGACCTTTTCAAAAATTCAGTATTTGGCTATGTAGCCAAA
CGCTTLAGTGCTTTTAAATCCTTTTGGCGATCGTGCTGATGCAGGTCAACAGTTAGCTAATTCTTATTTT
GCCATGGTCAATGGTGGTTGGTTTGGTCTAGGTCTTGGAAACTCGATTGAAAAACGAGGTTATTTGCCAG
AAGCTCATAACAGACTTTGTCTTTTCTATCGTGATTGAAGAATTTGGCTTTGTTGGTGCCAGTCTTATTTTAG
CTCTCTTGTTTTTCATGATTTTGGCGATTATCTTGGTCCGTATTCGAGCGGAGAATCCTTTCAATGCCATGG
TTGCACTCGGTGTGCGGAGGGATGATGTTGGTTCAGGTATTTGTCAATATCGGAGGGATTTCGGGCTTGATT
CGATCTACAGGAGTAACCTTCCCCTTCTTATCCCAGGGTGGAAATAGTCTTCTAGTCTTATCAGTGGCAGT
ACCTTTGTCTTAAATATTGATGCCAGTGAAAAACGGCGCTAAGTTGTACCGAGAATTGGAAAAATCAACCA
ATGAACCTTCTGTTGAAGCTCGAGCACCACCACCACCACCTGA

2 CFE38 "homologue of SEQ. ID NO. 34"

Fig 59
ATGCTCGGAATTTTAACCTTTATTCTGGTTTTTCGGGATTATTTAGTGGTGCACGAGTTCGGGGCACTTCTA
CTTTGCCAAGAATCAGGGATTTTAGTACGTGAATTTGCCATCGGTATGGGACCTAAAATTTTGTCTCACA
TTGCCAAGGATGGAACGGCCTATACCATTGCAATCTTGCTCTGGGTGGCTATGTCCGCATGGCCGGTTG
GGGTGATGATACAACCTGAAATCAAGACAGGAACGCCTGTTAGTTTGACACTTGCTGATGATGGTAAGGTT
AAACGGATCAATCTCTCAGGTAAAAAATTGGATCAAAACAGCCCTCCCTATGCAGGTGACTCAGTTTGATT
TTGAAGACAAGCTCTTTATCAAAGGATTGGTTCTGGAAGAAGAAAAAACATTTCAGTGGATCAGGATGC
AACGGTTGTGGAAGCAGATGGTACTGAGGTTCGGATTGCACCTTTAGATGTTCAATATCAAAAATGCGACT
ATCTGGGGCAAACTGATTACCAATTTTGCAGGTCCCTATGAACAATTTTATCTTAGGTGTCTGTTGTTTTT
GGTTTTAATCTTTATGCAGGGTGGTGTGAGAGATGTTGATACCAATCAGTTCCATATCATGCCCAAGGTG
CCTTGGCCAAGGTAGGAGTACCAGAAACGGCACAATTAACCAAGATTGGCTCAGATGAGGTTAGCAACT
GGGAAAGCTTGATCCAAGCTGTGGAACAGAAACCAAGATAAGACGGCACCGACTTTGGATGTGACTA
TTTCTGAAAAGGGGAGTGACAAACAAGTCACTGTTACACCCGAAGATAGTCAAGGTCTGTTACCTTCTAGG
TGTTCACCGGGGGTTAAGTCAGATTTTCTATCCATGTTTGTAGGTGGTTTTACAACCTGCTGCTGACTCAG
CTCTCCCAATTTCTCTCAGCTCTGAAAAATCTGATTTTCCAACCGGATTGGAACAAGTTGGGTGGACCTGTT
GCTATCTTTAAGGCAAGTAGTGATGCTGCTAAAAATGGAATTGAGAATATCTTGTACTTCTTGGCAATGA
TTTCCATCAATATIGGGATTTTTAATCTTATTCGATTCCAGCCTTGGATGGTGGTAAGATTGTGCTCAAT
ATCTAGAAAGCCATCCGCCGCAACCAATTGAAACAAGAAATTGAAACCTATGTCACCTTGGCCGGAGTG
GTGATCATGGTTGTCTTGATGATTGCTGTGACTTGGAAATGACATTATGCGACTCTTTTTTAGACTCGAGCA
CCACCAGCACCACTGA

2 CFE39 "homologue of SEQ. ID NO. 35"

Fig 60
ATCTACCCATATTTAAAAGGAATCATTACCAAAATTAAGTCCAAATACATTGTTCTTGAAACCAATGGTA
TTGGTTATATCTGCAATGTGGCCAATCCTTATGCCTATTCAGGTCAGGTTAATCAGGAGGCTCAGATTTAT
GTGCATCAGGTTGTGCGTGAGGACGCCCAATTTGCTTTATGGATTTCGCTCAGAGGATGAGAAAAAGCTCT
TTCTTAGTCTAATTTGGGTCTCTGGGATTGGTCTGTATCAGCTCTTGCTATTATCGCTGCTGATGACAATG
CTGGCTTGGTTCAAGCCATTGAAACCAAGAACATTACCTACTTGACCAAGTTCCCTAAAATTGGCAAGAA
AACAGCCAGCAGATGGTGTGCTGGACTTGAAGGCAAGGTAGTAGTTGCAGGAGATGGCCTTCCCTGCCAA
GGTGCAGTGCAAGCAAGTGCTGAAAACCAAGAAATTGGAAGAAGCTATGGAAGCCATGTTGGCTCTGGG
CTACAAGGCAACAGAGCTCAAGAAAAATCAAGAAATTTCTTTGAAGGAACGACAGATACAGCTGAGAACTA
TATCAAGTGGGCCCTTAAAATGTTGGTCAAACCTCGAGCACCACCACCACCACCTGA

2 CFE40 "homologue of SEQ. ID NO. 36"

ATGAAGAATAATCGTATTTTAGCACTTTCTGGAAATGATATTTTATAGTGGTGGTGGACTGTCAGCTGATT
GGCTACCTATACCTTGAACGGCTTGCATGGGTTTGTAGCAGTGACTTGTGTTGACAGCCTTGACAGAAAAA
GGATTGAAGTCTTTCCAACCTGATGATACCATTTTCAACATGAATTAGATAGCTTGGCTGATGTGGAATT
TCGGGGAATTAAGATTGGTCTTCTCCCTACTGTCAGTGTGGCTGAGAAGGCCTTGGACTTTATCAAACAA
CCCCAGGAGTACCTGTGGTGTGGATCCTGTCTTGGTCTGCAAGGAAACGCATGATGTAGCTGTCAGTO
ACCTCTGCCAAGAGTTGATTGCTTTTCCCTTATGTCAGTGTGATTACGCCTAATCTCCCAGAAGCAGAA
TTATTATCCGCTCAGGAAATTAAACCTTGGAAAGACATGAAAACCTGCAGCGCAGAAATTGCATGATTAG
GAGCGCCAGCAGTCATTATCAAGGGAGGCAATCGTCTTAGTCAGGACAAGGCTGTGGATGTCTTTTATGA
TGGACA GACCTTTACTATCCTAGAAAATCCAGTTATCCAAGGCCAAAATGCTGGTGCAGGTTGTACCTTT
GCCTCTAGCATTGCCAGTCACTTGATTAAAGGTGATAAACTTTTGCCAGCAGTAGAAAAGCTCTAAGGCTT
TCGTTTATCGTCTATTGCACAAGCAGATCAGTATGGAGTAAGACAATATGAAGCAAACAAAAACAACC
TCGAGCACCAACACCACCACCACTGA

2 CFE41 "homologue of SEQ. ID NO. 37"

ATGATIGAAAACGGAGAAAAAAGAGGAGCGAGTCCTGCTGATTGGTGTGGAATTGCAGGGTATGGACAGT
TTTGACCTCTCATGGAAGAATTGGCTAGTTTAGCGAAAACGGCAGGGGGCAGTCGTTGTAGATAGCTACA
GACAAAACCGTGAAAAATATGATTCCAAGACCTTCGTCGGCTCTGGTAAGTTGGAAAGAGATTGCGCTTAT
GGTGGATGCAAGAAGAAATCACTACTGTCATCGTCAACAACCGTCTGACCCCAAGGCAGAAATGTCAATCTA
GAGGAAGTTCTCGGTGTTAAGGTCAATTGACCGTATGCAGTTGATTTTGGATATCTTTGCCATGCGGGCTCG
AAGCCATGAAGGGAAGCTCCAAGTCCACCTAGCCCAACTCAAATACCTCTTGCTCGCTTGGTTGGTCAG
CGGATTATGCTCAGCCGTCAGGCAGGGGGAATTGGTTCCCGTGGTCTGGTGAAAGCCAACCTGGAGCTG
AACCGTCTGTAACGTTGCAATCAAATCACGGATATCGAGCGCCAGCTTAAGGTGGTTGAGAAAAATCGT
GCGACTGTCAAGAAAAACGTTTGGAGTCTAGCACTTTTAAGATTGGTTTGGTTTATACTAATGCTG
GGAAATCAACTATCATGAACATCTTGACCAGTAAGACCCAGTATGAAGCAGATGAGCTCTTTGCGACTCT
GGATGCGACAACCAAGAGTATTCATCTGGGAGGCAACCTCCAAGTAACCTTGAACAGATACCGTTGGCTTT
ATCCAAGATTGCGGACAGAGTTGGTGTCCAGTTTCAAGTCAACCTTGGAAAGAAAGCAAGCATGTGGACC
TTCTGGTTTATGTTATCGATGCTAGCAATCCTTACCACGAGGAGCATGAAAAACGGTTCTCTCCATCATG
AAAGACCTGGACATGGAAGATATTCCTCACTTGACGCTTTATAATAAAGCGGATTTGGTGGAGGATTTCA
CGCTACCCAAACGCCATATACCTCATTTCTGCCAAGTGTGAGGACAGTCGTGAAAACCTTGCAAGCATT
ATTGCTAGATAAGATTAAGGAAATTTTGAAGCATTACCTGCGAGTGCCTTTTCAAAGTCTTACAAG
ATTGATGATTAGAGAGTGTGCAATTCTGGAAGAAGCGTGATTATCAGGAAGACGGCGAAGTGATTACAG
GCTACATTTCCGAGAAAAATAAATGGAGGTTAGAAGAATTTTATGACCTCGAGCACCAACCACCACCA
CTGA

2 CFE42 "homologue of SEQ. ID NO. 38"

ATGGCAAAAAACATATCCTATGACCCTTGAGGAAAAGGAGAAACTTGAAAAAGAATTAGAAAGAATTG
AAATTGCTTCGTCGACCAGAAGTGGTAGAACGCATTAAGATTGCCCGTTTACATACGGTGATCTTTAGAAA
ACAGTGAGTACGAAGCAGCTAAGGATGAACAAGCCTTTGTGCAAGGACAAATCTCTAGCTTAGAAACAA
AAATCCGCTATGCTGAAATCGTCAATAGCGACGCAGTTGCCAGGACGAAGTAGCGATTGGTAAACAA
TCACCATCCAAGAAATTGGTGAGGACGAAGAAGAAGTTTATATTATCGTAGGTTTACGCTGGTGGGATGC
CTTTGCAAGGTAAAGTTTCAAATGAAAGCCCAATTGGGCAGGCCTTGATTGGCAAGAAAAACAGGTGACAC
AGCAACCATTGAAACGCCTGTTGGTAGCTATGATGTAAAAATCTTGAAGGTTGAAAAAACAGCCCTCGA
GCACCAACCACCACCACCACTGA

2 CFE43 "homologue of SEQ. ID NO. 39"

ATGACCAAAATTAATTGTAGGCTTGGGAAATCCAGGGGATAAATATTTTGAAACAAAACACAATGTTGGTT
TTATGTTGATTGATCAACTAGCGAAGAAACAGAAATGTCACCTTTACACACGATAAGATATTTCAAGCTGA
CCTAGCATCCTTTTCTCTAAATGGAGAAAAAATTATCTGGTTAAACCAACGACCTTTATGAATGAAAGT
GGAAAAGCAGTTTATGCTTTTAACTTACTATGGTTTGGATATTGACGATTTACTTATCATTACGATGA
TCTTGACATGGAAGTTGGGAAAATTCGTTTAAAGAGCAAAAGGCTCAGCAGGTGGTCAATAATGGTATCAA
GTCTATTATTCAACATATAGGAACTCAGGTCTTTAACCCTGTTAAGATTGGAATTGGAAGACCTAAAAAT
GGTATGTCAGTTGTTTATCATGTTTGTAGTAAGTTTGACAGGGATGATTATATCGGTATTTTACAGTCTAT
TGACAAAGTTGACGATTCTGTAAACTAGTATTTACAAGAGAAAAAATTTGAGAAAACAATGCAGAGGTA
TAACGGACTCGAGCAGCACCACCACCACCACTGA

2 CFE44 "homologue of SEQ. ID NO. 40"

ATGATTTTAAATTACAGGGGCAAATGGCCAATTAGGAACGGAACCTTCGCTATTTATTGGATGAACGTAATG
AAGAATACGTGGCAGTAGATGTGGCTGAGATGGACATTACCGATGCAGAAATGGTTGAGAAAGTTTTTG
AAGAGGTGAAACCGACTTTAGTCTACCACTGTGCAGCCTACACCGCTGTTGATGCAGCAGAGGATGAAG
GAAAAGAGTGGACTTCGCCATCAATGTGACGGGGACAAAAAATGTCGCAAAAGCATCTGAAAAGCATG
GTGCAACTCTAGTTTATATTTCTACGGACTATGTCTTTGACGGTAAGAAACCAGTTGGACAAGAGTGGGA
AGTTGATGACCGACCAGATCCACAGACAGAATATGGACGCACTAAGCGTATGGGGGAAGAGTTAGTTGA
GAAGCATGTGTCTAATTTCTATATTATCCGTACTGCCTGGGTATTTGGAAATTATGGCAAAAACCTTCGTTT
TTACCATGCAAAATCTTGCGAAAACCTCATAAGACTTTAACAGTTGTAAATGACCAGTACGGTCCGCGAC
TTGGACTCGTACCTTGGCTGAGTTCATGACCTACCTAGCTGAAAATCGTAAGGAATTTGGTTATTATCATT
TCTCAAATGATGCGACAGAAGACACAACATGGTATGATTTTGCAGTTGAAATTTTGAAAGATACAGATGT
CGAAGTCAAGCCAGTAGATTCCAGTCAATTTCCAGCCAAAGCTAAACGTCCGCTAAACTCAACGATGAGC
GTGGCCAAAGCCAAAGCTACTGGATTTGTTATTCCAACCTTGGCAAGATGCATTGCAAGAATTTTACAAAC
AAGAAGTGAGACTCGAGCACCACCACCACCACCTGA

2 CFE45 "homologue of SEQ. ID NO. 41"

ATGAAACGTCTCTCGACTCTAGAGTCGATTATAGTTTGCTCTTGCCAGTATTTTTCTACTGGTCATCGGT
CTGGTGGCTATCTATATAGCCGTTAGTCATGATTATCCCAATAATATCTGCCCATTTTAGGGCAGCAGGT
CGCCTGGATTGCCTTGGGGCTTGTGATTGGTTTTGTGGTCAATGCTCTTAAATACAGAATTTCTTTGGAAGG
TGACCCCTTTCTATATATTTTAGGCTTGGGACTTATGATCTTGCCGATTGTATTTTATAATCCAAGCTTAG
TTGCATCAACGGGTGCCAAAAAAGTGGGTATCAATAAATGGAATTAACCTATTTCAACCGTCAGAATTTAT
GAAGATATCCTATATCCTCATGTTGGCTCGTGTCAATTGTCCAATTTACAAAGAAACATAAGGAATGGAGA
CGCACGGTTCCGCTGGACTTTTTGTTAATTTCTGGATGATTCTCTTACCATTCCAGTCTAGTTCTTTTA
GCACTTCAAAGTGACTTGGGGACGGCTTTGGTTTTTGTAGCCATTTTCTCAGGAATCGTTTTATTATCAGG
GGTTTCTTGGAATAATTATTATCCAGTATTTGTGACTGCTGTAACAGGAGTTGCTGGTTTCTTAGCTATCT
TTATTAGCAAGGACGGACGAGCTTTTCTTACCAGATTGGAATGCCGACCTACCAAATCAATCGGATTTT
GGCTTGGCTCAATCCCTTTGAGTTTGCCCAAACAACGACTTACCAGCAGGCTCAAGGGCAGATTGCCATT
GGGAGTGGTGGCTTATTTTGTGAGGGATTAAATGCTTCGAATCTGCTTATCCCAGTTCGAGAGTCAGATAT
GATTTTACGGTTATTGCAGAGATTTTGGCTTTATTGGCTCTGTCTGCTGTTATTGCCCTCTATCTCATGTT
GATTTACCGTATGTTGAAGATTACTCTTAAATCAAATAACCAGTTCTACACTTATATTCCACAGGTTTGA
TTATGATGTTGCTCTTCCACATCTTTGAGAATATCGGTGCTGTGACTGGACTACTTCTTTGACGGGGATT
CCCTTGGCTTTTCAATTCGCAAGGGGGATCAGCTATTATCAGTAATCTGATTGGTGGTTGGTTTTATCTG
ATGAGTTACCAGACTAATCTAGCTGAAGAAAAGAGCGGAAAAGTCCCATTCAAACGGAAAAAGGTTGTA
TTAAAACAAATTAACCTCGAGCACCACCACCACCACCTGA

2 CFE46 "homologue of SEQ. ID NO. 42"

ATGGGAAAAATCATCGGAATCACTGGGGGAATTGCCTCAGGTAAGTCAACTGTGACAAATTTTCTAAGAC
AGCAAGGCTTTCAAGCAGTGGATGCCGACGCAGTCGTCCACCAACTACAGAAACCTGGTGGTCGTCTGTT
TGAGGCTCTAGTACAGCACTTTGGGCAAGAAATCAATCTTGAAAACGGAGAACTCAATCGCCCTCTCCTA
GCTAGTCTCATCTTTTCAAATCCTGAAGAGCAAAAAATGGTCTAATCAAATTCAGGGGGAGATTATCCGTO
AGGAACCTGGCTACTTTGAGAGAACAGTTGGCTCAGACAGAAGAGATTTTCTTCATGGATATTCCCCTACT
TTTTGAGCAGGACTACAGCGATTGGTTTGCTGAGACTTGGTTGGTCTATGTGGACCGAGATGCCCAAGTA
GAACGCTTAATGAAAAGGGACCAGTTGTCCAAAGATGAAGCTGAGTCTCGTCTGGCAGCCAGTGGCCTT
TACAAAAAAGAAAGATTGCGCCAGCCAGGTTCTTGATAATAATGGCAATCAGAACCAGGTTCTTAATC
AAGTGCATATCCTTCTTGAGGGAGGTAGGCAAGATGACAGAGATCTCGAGCACCACCACCACCACCT
GA

2 CFE47 "homologue of SEQ. ID NO. 43"

ATGAGAAAAATGTTATCAATGGTGGATTACCACTGCAAGGTGAAATCACTATTAGTGGTGCTAAAAATA
GTGTGCTTGCCTTAATTCAGCTATTATCTTGGCTGATGATGTGGTGACTTTGGATTGCGTTCCAGATATTT
CGGATGTAGCCAGTCTTGTGGAATCATGGAATTGATGGGAGCTACTGTTAAGCGTTATGACGATOTATT
GGAGATTGACCCAAGAGGTGTTCAAAATATTCCAATGCCCTTATGGTAAAATTAACAGTCTTCGTGCATCT
TACTATTTTATGGGAGCCTCTTAGGCCGTTTTGGTGAAGCGACAGTTGGTCTACCGGGAGGATGTGATCT
TGGTCTCGTCCGATTGACTTACACCTTAAGGCGTTTGAAGCTATGGGTGCCACTGCTAGCTACGAGGGA
GATAACATGAAGTTATCTGCTAAAGATACAGGACTTCATGGTGCAAGTATTTACATGGATACGGTTAGTG
TGGGAGCAACGATTAATACGATGATTGCTGCGGTTAAAGCAAATGGTCTGACTATTATTGAAAATGCAGC

2 CFE 47 (Contd.)

CCGTGAACCTGAGATTATTGATGTAGCTACTCTCTTGAATAATATGGGTGCCCATATCCGTGGGGCAGGA
ACTAATATCATCATTATTGATGGTGTGAAAGATTACATGGGACACGTCATCAGGTGATTCCAGACCGCA
TTGAAGCTGGAACATATATATCTTTAGCTGCTGCAGTTGGTAAAGGAATTCGTATAAATAATGTTCTTTAC
GAACACCTGGAAGGGTTTGTGCTAAGTTGGAAGAAATGGGAGTGAGAATGACTGTATCTGAAGACAGC
ATTTTTCGAGGAACAGTCTAATTTGAAAGCAATCAATATTAAGACAGCTCCTTACCCAGGCTTTGCAA
CTGATTTGCAACAACCGCTTACCCCTCTTTTACTAAGAGCGAATGGTCGTGGTACAATTGTGATACGATT
TACGAAAACGCTGTAAATCATGTTTTTGAAGTACGAAAGATGGATGCGGATATTTTCGACAACAAATGGTC
ATATTTTGTACACGGGTGGACGTGATTACGTGGGGGCCAGTGTTAAAGCGACCGACTTAAGAGCTGGGGC
TGCAGTAGTGATTGCTGGGCTTATGGCTGAAGGCAAACTGAAATTACCAATATCGAGTTTATCTTACGT
GGTTATTCTGATATTATCGAAAAATTACGTAATTTAGGAGCGGATATTAGACTTGTTGAGGATCTCGAGC
ACCACCAACCACCACTGA

2 CFE48 "homologue of SEQ. ID NO. 44"

ATGTCAAGAAATTGAATTTTCACCATCTTTGATGACCATGGATTGGACAAATTCAAAGAGCAGATTACTTT
TTGAATGATAAAGTAGCATCTTATCATATCGATATTATGGATGGCCATTTTGTTCCTCAATATTACCTTGT
CTCCTTGGTTTATTCAAGAAGTTCAAAAAATTAGTGACACACCTTTATCAGTTTCATCTGATGGTCACAGAC
CCAACCTTTTGGGTAGATCAAGTTCTCGATTACAAATGTGAGTATATTTGTATTTCATGCTGAAGTTCTGAA
TGGTCTTGCTTTTCGTTTGATGATAAAATTCATGATGCAGGTCTAAAGGCTGGTGTGTCCTTAATCCTG
AAACACCTGTTTCTACAATCTTTCCTTACATTGATTTACTTGACAAAGTAACTATTATGACTGTAGATCCA
GCTTTTTCAGGACAACGCTTTTGGAGTCTACCTTGTATAAAATCCAAGAACTCCATCAGCTTAGAGTTCA
GAATGCTTATCACTACATCATTGAGATGGATGGTTCTTCGAGTCGTAAGACTTTCAAACAAATTGATGTG
GCAGGACCAGATATTTATGTTATAGGTGCGCAGTGGATTATTGGTTTGGATGACGATATTGCCAAAGCCT
GGGATATCTGTTCTAGAGATTACGAAGAAATGACCGGAAAAACAATGCCAATCAAACCTCGAGCACCACC
ACCACCAACTGA

2 CFE49 "homologue of SEQ. ID NO. 45"

ATGAGAAATATGGCTTTGACAGCAGGTATCGTTGGTTTGCCAAACGTTGGTAAATCAACACTATTTAATG
CAATTACAAAAGCAGGAGCAGAGGCAGCAAACTACCCATTTGCGACTATTGATCCAAATGTTGGAATGG
TGGAAGTTCCAGATGAACGCCTACAAAACTAACTGAAATGATAACTCCTAAAAAGACAGTTCCCAACA
CAITTTGAATTTACAGATATTGACAGGGATTGTAAAAGGAGCTTCAAAGGAGAAGGGCTAGGGAATAAAT
TCTTGGCCAATATTCGTGAAGTAGATGCGATTGTTACGTAGTTTCGTGCTTTTGATGATGAAAATGTAATG
CGCAGCAAGGACGTGAAGACGCCTTTGTAGATCCACTTGCAGATATTGATACAATTAATCTGGAATTAA
TTCTTGCTGAGTTAGAATCAGTGAACAAACGATATGCGCGTGTAGAAAAGATGGCACGTACGCAAAAAG
ATAAAGAATCAGTAGCAGAATTCATGTTCTTCAAAGATTAAACCAGTCTTAGAAGACGGGAAATCAG
CTCGTACCATTGAATTAACAGATGAGGAACAAAAGGTTGTCAAAGGTCTTTTCTTTTGACGACTAAACC
AGTTCTTTATGTAGCTAATGTGGACGAGGATGTGGTTTCAGAACCTGACTCTATCGACTATGTCAAACAA
ATTCTGTAATTTGCAGCGACAGAAAATGCTGAAGTAGTCGTTATTTCTGCGCGTGCTGAGGAAGAAATTT
CTGAATTTGGATGATGAAGATAAAAAAGAGTTTCTTGAAGCCATTGGTTTGACAGAATCAGGTGTAGATAA
GTTGACCGCGTGCAGCTTACCACTTGCTTGGATTGGGAACTTACTTCACAGCTGGTGAAAAAGAGTTTCGC
GCTTGGACTTTCAAACGTTGGTATGAAGGCTCCTCAAGCAGCTGGTATTATCCACTCAGACTTTGAAAAAG
GCTTTATTCGTGCAAGTAAACCATGTCATATGAAGATCTAGTGAAATATGGATCTGAAAAGGCCGTAAAGA
AGCTGGACGCTTGCCTGAAGAAGGAAAAGAAATATATCGTTCAAGATGGCGATATCATGGAATTCCGCTTT
AATGTCCTCGAGCACCACCACCACCACCACTGA

2 CFE50 "homologue of SEQ. ID NO. 46"

ATCGAAATCGAAAAACCAATCGTATGAATGCGCTCTTTGAATTTTATGCGGGCGCTTTTGACAGATAAGC
AAATGAATTATATCGAGCTCTACTACGCTGATGATTACAGCCTTGCTGAAATTGCCGAGGAGTTCCGGTGT
CACTCGTCAGGCTGTCTATGACAATATCAAGCGAACAGAAAAGATTCTGGAAGATTATGAGATGAAATT
GCACATGTACTCGGACTATATTGTCCGCACTCAGATTTTGTATCAGATTTTGGAGCGCTATCCCAAGGATA
ACTTTCTGCAAGGAGCAGATAGAAATTTTAAACAAGCATTGATAATAGAGAACTCGAGCACCACCACCACC
ACCACTGA

2 CFE51 "homologue of SEQ. ID NO. 47"

ATGACCTTAGAATGGGAAGAATTTCTAGATCCTTACATTCAAGCTGTTGGTGAGTTAAAGATTAAACTTC
GTGGTATTCGTAAGCAATATCGTAAGCAAAATAAGCATTCTCCAATTGAGTTTGTGACCGGTGAGTCAA
GCCAATTGAGAGCATCAAAGAAAAATGGCTCGTCGTGGCATTACTTATGCGACCTTGGAACACGATTTG

2 CFE 51 (contd)

Fig. 72 (contd)
CAGGATATTGCTGGCTTACGTGTGATGGTTCAAGTTTGTAGATGACGTCAAGGAAGTAGTGGATATTTTGC
ACAAGCGTCAGGATATGCGAATCATACAGGAGCGAGATTACATTACTCATAGAAAAGCATCAGGCTATC
GTTCCATCATGTGGTAGTAGAATATACGGTTGATACCATCAATGGAGCTAAGACTATTTTGGCAGAAAT
TCAAAATTCGTACTTTGGCCATGAATTTCTGGGCAACGATAGAACATTCTCTCAACTACAAGTACCAAGGG
GATTTCCAGATGAGATTAAAGAAGCGACTGGAAATTACAGCTAGAATCGCCCATCAGTTGGATGAAGAA
ATGGGTGAAATTCGTGATGATATCCAAGAAGCCCAGGCACTTTTGTATCCTTTGAGTAGAAAATTAATG
ACGGTGTAGGAAACAGTGACGATACAGATGAAGAATACAGGCTCGAGCACCACCACCACCACCTGA

2 CFE 52 "homologue of SEQ. ID NO. 48"

Fig. 73
ATGGAACTTAATACACACAATGCTGAAATCTTGCTCAGTGCAGCTAATAAGTCCCACTATCCGCAGGATG
AACTGCCAGAGATTGCCCTAGCAGGGCGTTCAAATGTTGGTAAATCCAGCTTTATCAACACTATGTTGAA
CGGTAA GAATCTCGCCCGTACATCAGGAAAACCTGGTAAACCCAGCTCTGAACTTTTTTAACATTGAT
GACAAATGCGCTTTGTGGATGTGCCTGGTTATGGCTATGCTCGTGTCTTCTAAAAAGGAACGTGAAAAGT
GGGGGTGCATGATTGAGGAGTACTTAACGACTCGGGAAAATCTCCGTGCGGTTGTCAGTCTAGTTGACCT
TCGTTCATGACCCGTCAGCAGATGATGTGCAGATGTACGAATTTCTCAAGTATTATGAGATTCCAGTCATC
ATGTGGCGCAACCAAGGCGGACAAGATTCTCGTGGTAAATGGAACAAGCATGAATCAGCAATCAAAAAG
AAATTAACCTTTGACCCAAGTGACGATTTTCATCTCTTTTCATCTGTGCAAGGCAGGGATGGATGAGG
CTTGGGATGCAATCTTAGAAAAATTGGCGGCGCACTCGAGCACCACCACCACCACCTGA

2 CFE 53 "homologue of SEQ. ID NO. 49"

Fig. 74
ATGAAAACAAGAAAAATCCCTTTGCGCAAGTCTGTTGTGTCTAACGAAGTGATTGATAAGCGTGATTTCG
TCCGCAITGTCAAGAACAAAGGAAGGACAAGTCTTTATTGATCCTACGGGCAAGGCCAATGGCCGCGGGC
CTTATATCAAACCTAGACAATGCAGAAGCCCTAGAGGCGAAAAAGAAGAAGGTCTTTAACCGCAGCTTA
GCATGGAAGTGGAAGAAAGCTTTTATGACGAGTTGATCGCTTATGTGGATCACAAGTGAAAAGAAGAG
AGTTGGGACTTGAACCTCGAGCACCACCACCACCACCTGA

2 CFE 54 "homologue of SEQ. ID NO. 50"

Fig. 75
ATGTTAAACCCCTCTATTGATACCTTGCTCGACAAGGTTCCCTTCAAATATTCACCTCGTAATCTTGGAAAGC
AAAACGTGCCACGAATTGGAAGCAGGTGCCCCAGCAACTCAAGGTTTCAAGTCTGAAAAATCAACTCTT
CGCCTTTAGAAGAAATCGAATCAGGAAACGTTACAATTCAACCAGATCCAGAAGGAAAACGTGAAGCA
GTGCGTGGCGGTATCGAAGAAGAAAAACGCCGCAAGAAGAAGAAGAAAATCAAAGAGCAAAT
TGCTAAAGAAAAAGAAGATGGTGAAAAAATTCTCGAGCACCACCACCACCACCTGA

2 CFE 55 "homologue of SEQ. ID NO. 51"

Fig. 76
ATGTCATTAAACATCAAAACAACGTGCCTTCTCAACAGCCAGGCACACACCCTCAAACCTATCATCCAAA
TCCGGGAAAAATGGACTCAACGACCAAATCAAAACCAGCGTCCGTCAAGCTCTTGATGCGCOTGAATTAA
TCAAGGTACTCTCTTACAAAACACAGATGAAAACATCCACGAAGTAGCTGAAATTTTGGGAAGAAGAAA
TCCGTGTGGATACAGTCCAAAAAATAGGACGCATCTTGATTTTGTTTAAACAATCTAGCAAGAAAGAAAA
TCCCAAGATTCTAAGAAAGTCAAAGAAATCCTCGAGCACCACCACCACCACCTGA

2 CFE 56 "homologue of SEQ. ID NO. 52"

Fig. 77
ATGCGGATTGAAAATTATATACCAGATTTTGTGTGGAAGCAGTCTATGATCTGACAGTCCCAAGCCTGC
AGCGCGCAGGGAATCAAGGCTGTTTTGTGCGATTGTTGGATAATACCCTCATTGCTTGGAAACAACCTGATGG
AAGGCCAGAGATGAAGCAATGGCTACATGACCTTCGGGACGCGGGTATTGGCATTATCGTAGTGTCAAAT
AAGACCAAAAAACGCGTTCAACGAGCAGTTGAGAAATTTGGGATTGATTACGTTTACTGGGCCTTGAAGC
COTTCACATTTGGTATTGACCGTGCTATGAAGGAATTCACCTATGACAAAAAGGAAGTGGTCATGGTTGG
CGACCACTCATGACAGATATACGAGCAGCCACCCTGCAAGGATTCCGGTCAATTTTAGTCAAACCCCTTG
GTCCAACATGACTCAATCAAAACGCAGATTAACCGAACTCGTGAGCGTCTGTTATGAGAAAAATCACTG
AAAGTACGGACCGATTACATATAAAAAAGGAATTCTCGAGCACCACCACCACCACCTGA

2 CFE 57 "homologue of SEQ. ID NO. 53"

Fig. 78
ATGTTTCBAAAAATTTTAATTGCCAATCGTGGTGAAATTGCGGTTCTGATTATCCGTGCGGCACGTGAATT
GGGGATTGCGACGGTAGCGGTTTATTCAACTGCTGATAAGGAAGCTCTTCATACGCTTTTGGCAGATGAA
GCAGTTTGTATTGGTCCCTGGCAAGGCAACAGAGTCTTATCTCAATATTAATGCAGTTCTATCAGCTGCAOT
CTTGACTGAGGCAGAAGCTATTCACCCTGGTTTTGGATTCTCAGTGAAAATTCCAAATTTGCGACCATGT

2 CFE 57

GTGAAGAAGTAGGTATCAAGTTTATCGGTCCATCTGGTCAATGTTATGGATATGATGGGGGATAAGATCAA
TGCCCGTGCTCAGATGATTAAAGCAGGTGTGCCTGTTATACCAGGTTTCAGATGGAGAAGTGCATAACTCT
GAAGAAGCTTTGATTGTTGCTGAAAAAATTGGCTATCCTGTTATGCTCAAGGCTTCAGCAGGTGGAGGTG
GTAAACGGATTTCGTAAAGTTGAAAAACCAGATGACCTCGTTTCTGCCTTTGAAACTGCCTCTAGTGAGGC
CAAGGCCAATTATGGCAATGGTGCCATGTACATAGAACGGGTTATCTATCCAGCTCGGCACATTGAGGTT
CAAAATCTAGGTGATGAGCATGGACATGTGATTCACTTGGGTGAACGGGATTGTTCTCTTCAAAGGAATA
ACAAAAGGTTTTGAAAGAAAGTCCCTCGATTGCAATCGGAAAAACGCTGCGTCATGAAATAGGTGCTG
CTGCTGTTTCGAGCGGCAGAGTTTGTGGCTATGAGAATGCAGGAACCATTTGAATTTCTTCTTGATGAAGC
AAGTACAAAATTTCTATTTTCATGGAGATGAATACTCGTGTTCAGGTAGAACATCCAGTAACAGAGTTTOTT
TCAGGTGTTGATATCGTTAAGGAACAGATTTGCATTGCGGCAGGTTCAGCCTTTGTCTGTTAAGCAAGAAG
ATATTGTCCTACGCGGTTCATGCCATCGAGTGTCTGATCAATGCAGAAAACCCAGCCTTTAACTTTGCTCCA
AGTCCAGGTAAGATTACTAATCTCTATCTGCCAAGTGGTGGAGTTGGCTTGGCGGTGGATTTCAGCAGTTT
ATCCAGGTTATACCATTCCGCCTTATTATGATAGTATGATTGCCAAAATCATAGTACACGGCGAAAATCG
TTTTGACGCTTGATGAAAATGCAACGTGCCCTCTATGAATTAGAGATTGAAGGAGTGCAGACCAATGCA
GATTTCCAGCTTGATCTCATTTCAGATCGCAATGTCATTGCTGGGGATTATGATACTTCTTCTTGATGGA
AACCTTCTTACCTAAATATCAAGAAAAAGAACTCGAGCACCACCACCACCACCCTGA

2 CFE 58 "homologue of SEQ. ID NO. 54"

ATGATTACAAAGTTTTTTATCAAGAAACAAAAGAACGTAGCCACGCGGTGAAACAACACGCACGCTTT
ACCTAGACATCGATGCCAGCTCAGAACCTTGAGGGCCGTATCACTGCTCGCCAACTTGTGCAAGAAAAATCG
CCAGAGTACAATATCGAGTATATCGAACTCTTGTCTGACAAATTGCTCGATTACGAAAAAGAACTGGC
GCCTTCGAAATTACGGAGTTCTTCGAGCACCACCACCACCACCCTGA

2 CFE 59 "homologue of SEQ. ID NO. 55"

ATGAAGGATAGATATATTTTAGCATTGAGACATCCTGTGATGAGACCAGTGTGCGCGTCTTGAAAAACG
ACGATGAGCTCTTGTCCAATGTCATTGCTAGTCAAATTGAGAGTCAACAACGTTTTGGTGGCGTAGTGCC
CGAAGTAGCCAGTGTGTCACCATGTGCGAGGTTCATTACAGCCTGTATCGAGGAGGCATTGGCAGAAGCAGG
GATTACCGAAGAGGACGTGACAGCTGTTGCGGTTACCTACGGACCAGGCTTGGTGGGAGCCTTGCTAGTT
GGTTGTGAGCTGCCAAGGCCCTTGTCTGGGCTCAGGACTTCCACTGATTCTGTTAATCATATGGCTGG
GCACCTCATGGCAGCTCAGAGTGTGGAGCCTTGGAGTTTCCCTTGCTAGCCCTTTTAGTCAGTGGTGGGC
ACACAGAGTTGGTCTATGTTTCTGAGGCTGGCGATTACAAGATTGTTGGGGAGACACGAGACGATGCAGT
TGGGGAGGCTTATGACAAGGTGCGTGTGTCATGGGCTTGACCTATCCTGCAGGTGCTGAGATTGACGAG
CTGGCTCATCAGGGGCGAGGATATTTATGATTTCCTCCCGTGGCCATGATTAAGGAAGATAATCTGGAGTTCT
CCTTCTCAGGTTTGAAATCTGCCCTTATCAATCTTCATCACAATGCCGAGCAAAAGGGAGAAAGCCTGTC
TACAGAAGATTGTTGTGCTTCTTCCAAGCAGCAGTTATGGACATTCTCATGGCAAAAACCAAGAAGGCT
TTGGAGAAATATCCTGTTAAACCCCTAGTTGTGGCAGGTGGTGTGGCAGCCAATAAAGGTCTCAGAGAAC
GCCTAGCAACTGAAATCACAGATGTCAATGTTATCATTCCACCTCTGCGTCTGTGCGGAGACAATGCAGG
TATGATTGCTTATGCCAGTGTGAGCGAGTGAACAAAGAAACTTTGCAAACTTGGACCTCAATGCCAAA
CCAAGTCTTGCTTTGATACCATGGAACCTCGAGCACCACCACCACCACCCTGA

2 CFE 60 "homologue of SEQ. ID NO. 56"

ATCTGTGGAATTGTGGTGTGTTGGTGGAAACACAAATGCAACTGATATTTTGATTCAAGGGCTTGAAAAGC
TTGAATACCGTGGCTATGATTCTGCGGGAATTTTGTCTAGATGGTGTGATAACCATTTGGTGAAGGCT
GTTGGTCTATGCGCAAAATTGTCTGCCAAGACAGCTGGTGTGAGGGGAACAACCTGGTATCGGACATACTC
GTTGGGCAACTCATGGGAACCAACGGAAGACAATGCTCACCCACACCGCTCTGAGACAGAACGTTTTG
TCTTGGTTTCAAAATGGGGTGATTGAAAACTACCTTGAAATTAAGAAGAAATACCTTGCTGGGCACCACTT
CAAAGGGCAAAACAGATACGGAATCGCCGTACATTTGATTGGAAAAATTGCGGAAGAAGACGGTCTCTC
ACTTCTTGAAGCCTTTAAAAAAGCTCTTCATATTATCCGTGGTTTCAATGCTTTGCTTGAATTGACTCTG
AAAATCCAGATGTCTATGTAGCGAAAAACAAATCTCCACTTTTGATTGGTCTTGGGGAAGGCTACAA
TATGGTCTGCTGAGATGCTATGGCTATGATTGCTGAAACCAACCAATACATGGAATTCATGACCAAGAG
TTGGTAATCGTCAAGGCTGATAGCGTGGAAAGTTCAAGACTATGATGGTAACAGTCTGTAACGTGCTAGCT
ATACTGCGGAACCTTGACTTGTGAGATATCGGTAAGGGAACTTATCCTTACTACATGCTTAAGGAATTTGA
TGAGCAACCAACTGTTATGCGTAAACTCATTCAAGCCTACACGGATGATGCTGGTCAAGTAGTGATTOAT
CCTGCTATCATTAAGGCTGTTCAAGACGCGAGACCGCATCTACATCCTTGCAAGCTGGAACATCTTACCATG
CAGGATTGCTTCTAAGAAAAATGTTGGAAGAATTGACAGATACACCAGTTGAACCTTGGCATCTCATCTGA
GTGGGGGTACGGTATGCCACTTCTCAGCAAGAAACCACTCTTCATCTTTATCAGCCAATCTGGTGAACA

2 CFE 60 (cont'd)

GC GGATAGT CGTCAAGT TTTGGTCAAGGCTAATGAAATGGGAATTCCAAGCTTAACAGTGACAAACGTTTC
CAGGTTCAACCCCTCTCACGTGAAGCCAACTATACCATGCTCCTTEACGCAGGTCCTGAAATTGCCGTGGC
ATCAACTAAAGCCTATACAGCGCAAATCGCAGCCCTTGCCCTTCCTTGCAAAAGCAGTCGGAGAAGCAAAT
GGTAATGCTAAAGCGCAAGCCTTTGACCTGGTTTCATGAATTGTCAATCGTAGCTCAGTCTATCGAATCAA
CTCTTTCAAGAGAAAGAAACCAATTGAAGCCAAGGTTTCGTGAACCTTCTTGAAACAACCTCGTAACGCCTTTTA
CATCGGACGTGGTCAAGATTACTACGTAGCCATGGAAGCAAGTCTCAAACCTCAAAGAGATTTCCTTATATC
CAGTGTGAAGGTTTGGCGGCAGGAGAACTCAAGCACGGAACCAATTGCCTTGATTGAAGAAGGAACACCT
GTCTTGCTCTCTTGTGATCCAGTCCCTTGCCAACCACACTCGTGGAAATATCCAAGAGGTGGCAGCCC
GTGGTGCTAAGGTCCTCACTATCGCAGAAAGAAAATGTTGCTAAAGATACCGACGATACTCGTCTTACGAC
TGTACACCCCTTACCTCTACCAATTTCAATGGTTCGTACCGACGCAATTGGTTGCTTACTTTGCAACCCCTCC
ACCGTGGCCTCGATGTGGATAAACACGTAACCTTGCCAAGTCAGTAACGGTAGAACTCGAGCACCACC
ACCACCACCCTGA

2 CFE61 "homologue of SEQ. ID. NO. 57"

ATGATACGTATCGAAAATCTCAGTGTCTCCTACAAAGACACGTTGGCACTTAAGGATATTTCACTAGTGC
TCCATCGACCAACAATTACCGGCATCATTGGTCCAAACGGCGCTGGGAAATCAACACTATTAAAAGGTAT
GGTGGGAAATTATCCACATCAAGGTCAGGCATTTCTCGATGACAAGGAAGTTAAAAAATCCTTACACCGA
ATGGCTATGTCGAACAAAAAATCAATATCGACTACAACCTTTCCCATCAAGGTCAAGGAATGCGTCTCGT
TAGGACTATTTCCCTCTATTCCCTCTCTTTGGAAGTTTAAAGGCTAAACATTGGAAGAAAGTGCAAGAGGC
CCTTGAAATCGTCCGCCTAGCTGACTACGCTGAACGTCAAATTAGTCAACTGTCTGGAGGTCAATTCCAG
CGGGTCTTGATTGCCAGATGTTTGGTGCAGGAAGCCGACTATATCCTCTTGATGAACCCCTTTGCTGGGAT
TGACTCTGTGAGTGAAGAAATCATCATGAATACGCTGAGAGATTTGAAAAAAGCTGGGAAGACGGTTCT
CATCGTTACACACGACCTCAGCAAGATTCCCCACTACTTCGATCAAGTCTTACTTGTCAATCGAGAAGTG
ATTGCCCTTGGTCCAACAAAAGAACTTTTACCGAAACCAATCTAAAAGAAGCTTACGGTAATCAACTCT
TTTTCAATGGAGGTGACCTACTCGAGCACCACCACCACCACCCTGA

2 CFE62 "homologue of SEQ. ID. NO. 58"

ATGCCGAAAGAAGTGAATTTAACAGGCGAAGAAAGTTGTCGCTTTAACCAAAGAATATTTAACGGAAAG
GATGTTCAATTTTGTCCATAAGGCCTTGGTCTATGCTGTTGAATGCCACAGTGGTCAATATCGCAAATCAGG
CSAGCCCTATATCATTACCCCTATCCAAGTGGCAGGTATTTTAGCTAAGCTAAAGCTGGATGCTGTAAACA
GTAGCTTGTGGAATCTTGCATGATGTGGTGGAAAGATACAGATGCGACTTTGGACGATTGGAAAGAGAGT
TTGCTCTGATGTGCGGATGATTGTTGACGGAGTTACCAAGCTTGGCAAGGTGAGTACAAATCGATCGA
GGAGCAATTAGCGGAAATCATCGCAAGATGCTCATGGCCATGTCTGAGGACATCCGCGTTATTTGGTCT
AAACTGTCTGACCGCTTGCACAATATGCGGACCCTGAAACATCTTCGAAAAGACAAGCAGGAGCGTATTT
CCAAAGAAACCATGAAAATCTATGCCCGGCTTGCCCATCGTTTGGGGATTTCCAGTGTCAAATGGGAATT
AGAAAGACTTGTCTTTCCGTTATCTCAATCCAACGGAGTTTACAAGATTACCCATATGATGAAGGAAAAG
CGCAGGAGCGGTGAGGCCTTGGTGGATGAGGTAGTCACAAAATTAGAGGAGTATACGACAGAACGTCAC
TTGAAAGGGGAAGATTTATGGTCCGTCCTCAAGCATATTTACTCAATTTTCCGCAAAATGCAGGACAAGAGAA
AACGGTTTGAGGAAATCTATGATCTGATTGCTATTCGTTGTATTTTAGATACCCAAAGTGATGTTTATGCC
ATGCTTGGTTACGTGCATGAATTTTGGAAACCGATGCCAGGTGCGCTTCAAAGACTATATCGCCAACCGCA
AGGCCAATGGTTATCAGTCTATCCATACGACTGTTTATGGACCAAAGGGCCGATTGAATTCCAGATTCCG
AACCAAGGAAATGCACGAGGTGGCTGAGTACGGGGTGGCGGCTCACTGGGCTTATAAGAAAGGTATAAA
GGGCAAGTTAACAGCAAGGAATCAGCTATTGGAATGAACTGGATCAAGGAGATGATGGAGCTCCAAGA
CCAGGCTGATGATGCTAAGGAATTTGTGGAATCTGTTAAGGAAAACCTATTTGGCTGAGGAGATTACGTT
TTTACCCAGATGGAGGTGTCCGTTCCCTTCCCAAAGATTACAGGACCGATTGATTTTGCCTACGAAATCCA
TAGCAAAGTCCGTTGAAAAAGCAACTGGTGGCAAGGTCAATGGCCGATGGTTCCACTGACAACCAAGTT
AAAGACAGGGGATCAGGTTGAAATTAATCGCCAACCCGAACCTCTTTGGACCTAGCCGTGACTGGCTCAAT
ATGCTCAAGACTAGCAAGGCGCGCAATAAGATTCCGCCAGTTCTTTAAAACCAAGATAAGGAATTGTCT
GTCAACAAGGGTCTGTGAGATGCTGATGGCTCAGTTCCAAGAAAATGGCTATGTGGCAAATAAATTTATGG
AQAAGCCCAATGATCAAGTTCTGCAAAAGACCAAGTTACAAGACAGAAGACTCCCTCTTTGCGGCCAT
TGGTTTGGGGAAATCGGTGCGATTACCGTCTTTAACCGTCTGACTGAAAAGGAGCGCCGTGAGGAAGAG
CGTGGCAAGGCCAAGGCTGAGGCAGAGGAGCTTGTCAAAGGTGGCGAGGTCAAGGTTGAAAATAAAGA
AACTCTCAAGGTCAAGCATGAGGGGGGAGTGGTTATTGAAGGTGCTTCTGGTCTCTAGTGCGGATTGCT
AAGTGTGTAACCCCGTGCCTGGTGACGATATTGTTGGCTACATTACCAAGGGTCTGTTGTGGCTATTC
ACCGTGTGGACTGTATGAACCTGCGTGCCCAAGAAAACCTACGAGCAACGTCTCCTTGATGTGGAATGGGA
AGACCAGTACTCTAGCTCAAATAAGGAGTATATGGCCCATATCGATATCTACGGTCTCAACCGTACAGGA

2 CFE62 (Contd)

(Contd) Fig 83
CTGTTGAACGATGTACTGCAAGTTCTTTCAAATACAACCAAGAATATTTCAACGGTCAATGCCCAACCAA
CCAAGGATATGAAGTTTGCTAATATCCATGTGTCTTCGGTATTGCCAACCTCTCTACACTGACCACGGTT
GTCGATAAAATTAAGAGTGTGCCAGAAGTTTACTCTGTCAAACGGACCAACGGCCTCGAGCACCACCACC
ACCAACTGA

2 CFE64 "homologue of SEQ. ID NO. 60"

Fig 84
ATGACAGAAAGAAATCAAAAATCTGCAGGCACAGGATTATGATGCCAGTCAAATTCAAGTTTTAGAGGGC
TTAGAGGGCTGTTCTGATGCGTCCAGGGATGTACATTGGATCAACCTCAAAGAAGGTCTTCACCATCTAG
TCTGGGAAATTTGTTGATAACTCAATTGACGAGGCCTTGGCAGGATTGCGCAGCCATATTCAAGTTTTTATT
GAGCCAGATGATTGATTACTGTTGTGGATGATGGGCGTGGTATCCCAGTCGATATTCAGGAAAAAACAG
GTCGTCTGCTGTTGAGACCGTCTTTACAGTCCTTCACGCTGGAGGAAAGTTTCGGCGGTGGTGGATACAA
GGTTTCAGGTGOTCTTCACGGGGTGGGGTCTGTCAGTTGTTAATGCCCTTTCCTCACTCAATTAGACGTTTCATG
TCCATAAAAACGGTAAGATTTCATTACCAAGAATACCGTCTGTCATGTTGTGCGCAGATCTTGAAATAGT
TGGAGATACGGATAAAACAGGAACAACACTGTTCACTTCACACCGGACCCAAAAATCTTCACTGAAACAAC
AATCTTTGATTTTGATAAATTAATAAACGGATTCAAGAGTTGGCCTTTCTAAATCGCGGTCTTCAAATTT
CTATCACTGATAAGCGCCAAGGTTTGGAAACAACCAAGCATTATCATTATGAAGGTGGGATTGCTAGTTA
COTTGAAATATATCAACGAGAACAAGGATGTAATCTTTGATACACCAATCTATACAGACGGTGAGATGGAT
GATATCACAGTTGAGGTAGCCATGCAATACACAACGGGTACCATGAAAATGTCATGAGTTTCGCCAATA
ATATTGATACACATGAAGGTGGAACGCATGAACAAGGTTTCCGTACAGCCTTGACACGTGTTATCAACGA
TTATGCTCGTAAGAATAAGTTACTGAAAGACAATGAAGACAATCTAACAGGGGAAGATGTTTCGCGAAGG
CTTAAGTGCAGTTATCTCAGTTAAACACCCAAATCCACAGTTTGAAGGACAAACGAAGACCAAAATTGGGA
AATAGCGAAGTGGTCAAGATTACCAATCGCCTCTTCAGTGAAGCCTTCTCCGATTTCTCTCATGGAAAATC
CACAGATTGCCAAACGTATCGTAGAAAAAGGAATTTTGGCTGCCAAGGCTCGTGTGGCTGCCAAGCGTGC
GGGTGAAGTCACACGTAAAAAATCTGGTTTGGAAATTTCCAACCTTCCAGGGAACTAGCAGACTGTTCT
TCTAAATAACCCTGCTGAAACAGAACTCTTCATCGTCAAGGAGACTCAGCTGGTGGATCAGCCAAATCTG
GTCGTAAACCGTGAGTTTCAGGCTATCCTTCCAATTCCGGTAAGATTTTGAACGTTGAAAAAGCAAGTAT
GGATAAGATTCTAGCTAACGAAGAAATTCGTAGTCTTTTCACAGCCATGGGAACAGGATTGCGCGCAGAA
TTTGATGTTTCGAAAGCCCGTTACCAAAAACCTCGTTTGTGATGACCGATGCCGATGTGATGGAGCCCA
TTCTGTAACCTTCTTTTAAACCTTGATTATCGTTATATGAAACCAATCCTAGAAGCTGGCTATGTTTATATG
CCCAACCACTATCTATGGTGTCAAGGTTGGAAGCGAGATTAAAGAATATATCCAGCCGGGTGCAGATC
AAGAAATCAAACTCCAAGAAGCTTTAGCCCGTTATAGTGAAGGTGCTACCAAAACCGACTATTCAGCGTFA
TAAGGGGCTAGGTGAAATGGACGATCATCAGCTGTGGGAAACAACCATGGATCCCGAACATCGCTTGAT
CGCTAGAGTTTCTGTAGATGATGCTGCAGAAAGCAGATAAAATCTTTGATATGTTGATGGGGGATCGAGTA
GAGCCTCGTCTGAGTTTATCGAAGAAAAATGCTGTCTATAGTACACTTGATGTCTCTGAGCACCACCACC
ACCACCACTGA

2 CFE65 "homologue of SEQ ID NO. 61"

Fig 85
ATGGGATTTACTGAAGAAACAGTACGTTTAAATTGGACGATTCCAATAAAAAAGAAATTAGCGAAACTT
TGACAGATGTTTATGCTTCGTTGAACGATAAGGGTTACAACCCAATTAACCAAATCGTAGGTTACGTATT
GAGTGGAGACCCTGCCTACGTTCTCGTTATAATAATGCACGAAATCAAATCCGTAAGTATGAGCGTGAT
GAAATCGTTGAGGAATTGGTTTCGCTACTATCTCAAAGGACAAGGAGTGGATCTACTCGAGCACCACCACC
ACCACCACTGA

2 CFE66 "homologue of SEQ. ID NO. 62"

Fig 86
ATGGTCAACTATCCACATAAAGTTTCATCACAAAAAGACAAACATCTCTTTCTCAACCCAAAAATTTCC
CAATTCGAGGAATGTCCTTTTGAAGAAGATGATCAATGCTACCAACGACTACTATTTGTCTCAGGGCTTGGC
TGTTATACATAAGAAACCAACTCCTATTCAAATCGTACAAGTGGACTATCCACAACGAAGTCGTGCCAAG
ATTGTTGAAGCCTATTTTCGACAAGCTTCAACGACGGACTATTCTGGCGTTTATAATGATATTACATCOA
CTTTGAAGTCAAGGAACAACAAAAACGTTGCGATTCCGATGAAAAATTTTCATCCACATCAGATTGAG
CATATGGAACAAGTCCTTGCCCAACAAGGAATCTGCTTTGTCTCTTCACTTTTCTTCTCAGCAAGAAAC
CTACTTATTGCCGGCATTTCGATTTGATTTCGCTTCTATCATCAAGATAAGGGACAAAAATCAATGCCACTTO
AATATATTGGAATAATGATGATAAATCAAGGCTGGTGCCTTCCCTCAAATTCCTTATCTCAATGTTATC
AAAGAAGATTTATTAGGTGGTAAACAAGACTCGAGCACCACCACCACCACCACTGA

2 CFE67 "homologue of SEQ. ID NO. 63"

2 CFE 67 homologue of SEQ ID NO: 63

ATGGCTCTATTTAGTAAAAAAGATAAGTATATTCGAATCAATCCCAATCGTTCGGTTAGGGAAAAAECTC
AAGCTAAGCCAGAGGTTCCAGATGAATTATTTTCCCAGTGTCCAGGCTGTAAGCATACCATCTATCAGAA
GGATCTGGGAAGTGAACGTATCTGTCCGCACGTAGCTATACCTTTCTGATTTCTGCCCAAGAACGCTTGG
CTTTGACGATTGATATGGGAACCTTCAAAGAATTGTTTACAGGGATTGAAAGCAAGGATCCCTTGCATT
CCCTGGTTACCAAAAGAACTGGCATCTATGCGTGAAAAAACAGGTCTGCATGAAGCCGTTGTGACAGG
AACTGCTCTTATTAAAGGTCAGACTGTGGCTCTTGGGATTATGGATTCTAATTTTATCATGGCTTCTATGG
GTACGGTTGTAGGTGAAAAAATCACTCGTTTGTGTTGAGTATGCGACTGTCGAAAAATTGCCAGTTGTCT
ATCACAGCCTCTGTTGGAGCCCGTATGCAGGAAGGAATCATGAGTCTCATGCAGATGGCTAAGATCTCT
GCAGCGTTAAACGCCATTCAAATGCTGGTCTCTTTTACCTGACCATTTTGACAGATCCAACGACTGGTG
GTGTGACAGCTTCTTTCTGCTATGGAAGGCGATATCATTCTGGCTGAACCACAGAGCTTGGTTGGTTTGGT
GGCGCTCGTGTGATTGAAAAATACGGTTCTGTGAAAGCTTGCCTGAGGATTTCAAAAGGCAGAAATTCCTAT
TAGAACATGGCTTTGTGGATGCTATTGTCAAAGAAGAGACTTACCAGATACGATTGCTAGCCTAGTCAG
ATTGCATGGAGGGAGTCTAGACTCGAGCACCACCACCACCACCTGA

2 CFE68 "homologue of SEQ. ID NO. 64"

ATGAGAAATTAAGGATTGGACGTCGGTTCAAAAACGGTAGGGGTGGCGATTAGCGATCCGCTTGGTTT
CAGCTCAAGGGCTTGAAATCATCCAGATAAATGAAGAACAAGGCCAATTGGTTTGGACCGCGTTAAGG
AATTGGTTGATACTTACAAGGTGGAACGATTGTAGTGGGCTTGCCTAAAAACATGAACAATAACAAGTGG
ACCGCGCTAGAAAGCTAGTCAAGCCTACGGAGCAAAGCTAGAAGAGTTTTTTGGTTTACCAGTAGACTAT
CAGGATGAACGCTTGACAACAGTGGCTGCTGAGCGCATGTTGATTGAACAAGCAGATATCAGTCGCAAT
AAGCGCAAGAAAGTCATTGATAAGTTAGCAGCTCAGCTGATTTTACAAAATTATTTAGATAGAAAATTC
TCGAGCACCAACCACCACCACCACCTGA

2 CFE69 "homologue of SEQ. ID NO. 65"

ATGACAAAACCTTACTGTAAAGACGTTGACTTGAAAGGTAAAAAAGTCCTCCTTCGTGTTGACTTCAACG
TACCATTTGAAAGATGGCGTAATCACTAACGATAACCGTATCACAGCAGCTCTTCCAATTAAGTACAT
CATCGAAACAAGGTGGACGTGCAATTCTTTCTCTCACCTTGGACGTGTGAAAGAAGAATCTGATAAAGCT
GGTAAACACTTGTCTCTGTAGCAGCTGACTTGGCAGCAAACTTGGTCAAGATGTTGTTTCCCAGGTGT
CACTCGTGGTGCTGAATTGGAAGCGGCAATCAACGCTCTTGAAGATGGACAAGTTCTCTTGGTTGAAAAC
ACTCGTTACGAAGATGTTGACGGCAAGAAAGAATCTAAAAACGATCCTGAACCTTGGTAAATACTGGGCA
TCACTTGGAGATGGTATCTTCGTAAACGATGCATTCCGGTACAGCTCACCGTGCACACGCATCTAACGTTG
GTATCTCAGCAAACGTTGAAAAAGCAGTTGCTGGTTTCTTCTTGA AAAACGAAATTGCCTACATCCAAGA
AGCAGTTGAAACTCCAGAACGTCCATTCTGTGGCTATCCTTGGTGGTTCAAAAAGTTTCAGACAAGATCGGT
GTTATCGAAAACCTTGCTTGAAAAAGCTGATAAAGTCTTATCGGTGGTGGGATGACTTACACATTCTACA
AAGCACAAGGTATCGAAATCGGTAACCTCACTTGTAGAAGAAGACAAATTGGATGTTGCGAAAGCTCTTCT
TGA AAAAGCAAATGGTAAATTGATCTTGCCAGTTGACTCAAAAAGAAGCTAACGCATTTGCTGGTTACACT
GAAGTGCGTGACACTGAAGGTGAAGCAGTTTCTGAAGGCTTCTTGGTCTTGACATCGGTCCAAAATCTA
TCGCCAAATTTGACGAAGCTTTGACTGGTGCCAAAACAGTTGTATGGAACGGACCTATGGGTGTATTTGA
AAAACCCAGATTTCCAAGCTGGTACAATCGGTGTGATGGACGCTATCGTGAAACAACCAGGAGTTAAATC
AATCATCGGTGGTGGTGACTCAGCTGCCCGCAGCGATTAACCTTGGCCGTGCAGACAAGTTCTCATGGATT
AGTAGGGGTGGTGGAGCATCAATGGAACCTTCTTGAAGGTAAAGGTCTTCCAGGACTTGCAGCCTTGACAG
AAAAACTCGAGCACCACCACCACCACCTGA

2 CFE70 "homologue of SEQ. ID NO. 66"

ATGTTAAATCAGAAAAACAATCACGTTATCAAATGTTAAATGAAGAATTGTCCTTCCTATTGGAAGGCG
AAACCAATGTTTTGGCTAATCTTTCCAACGCCAGTGCTCTCATAAAATCACGTTTTCTAATACCGTATTT
GCAGGCTTTTATTTGTTTCGATGGAAAGGAATTGGTTTTAGGCCCTTCCAAGGAGGTGTTTCTGCATCCG
TATTGCACTAGGCAAGGGTGTGTTGTGGTGAGGCAGCTCACTTTCAGGAAACTGTTATTGTTGGAGATGTG
ACGAOCTATCTCAACTATATTTCTTGTGATAGTCTAGCTAAAAGTGAAATTGTGGTGCCGATGATGAAGA
ATGGTCAGTTACTTGGAGTTCTGGATCTGGATTCTTCAGAGATTGAGGATTACGATGCTATGGATCGAGA
TTATTTGGAACAATTTGTCGCTATTTTGCTTGAAAAGACAACATGGGACTTTACGATGTTTGAGGAAAAA
TCTCTCGAGCACCACCACCACCACCTGA

2 CFE71 "homologue of SEQ. ID NO. 67"

ATGAGAAATCGAACTATTGACTCCCTTTACCAAGGTAGAGTTGGAGCCAGAAATCAAGGAGAAAAAACGC
AAACAACCTGGGATTTTAGGGGGGAATTTTAACCTGTTCACAATGCCCATCTCATTGTTGCGGATCAAG

2 CFE 71 (Contd.)

Fig 91 (Contd.)
TACGGCAACAGTTGGGACTGGATCAAGTTCTTCTCATGCCTGAATACCAACCTCCTCACGTTGATAAAAA
GGAACCATCCCTGAACACCATCGTCTCAAGATGCTTGAGTTGGCAATTGAGGGGATTGACGGCCTAGTC
ATTGAAACCATTTGAGTTGGAGCGCAAGGGTATTTCTACACCTACGATACCATGAAGATTTTGACAGAGA
AGAATCCAGATACGGATTATTACTTTATCATCGGTGCCGACATGGTTGACTATCTGGCTAAGTGGTACCG
AATTGATGAACTGGTTGACATGGTTTCACTTTGTGGGGGGTTCAGCGTCCACGCTACAAGGTAGGGACTTCC
TATCCAGTTATCTGGGTGGACGTACCGCTCATGGATATCTCGTCCAGCATGGTGGGGGACTTCCTTGCCCA
AGGTCGGAAACCCAACTTTCTCCTACCTCAGCCAGTGCTAGACTACATCGAGAAGGAGGGGGCTCTACCTC
GAGCACCACCACCACCACCTGA

2 CFE72 "homologue of SEQ. ID NO. 68"

Fig 92
ATGAATATTGCAAAAATAGTCAAGAGAAGCGCGTGAGCAGAGTCGCTTGACAACCTTGGACTTTGCGACA
GGCATTTTTGATGAATTTATCCAATTACATGGTGACCGTTCTTTTCGTGATGATGGTGACAGTTGTTGGTGG
TATTGGTTGGCTTGGAGACCAAGCTGTAACAGTGGTTGGTATCCAAAAAGGCAAGAGTTTGCAAGACAA
CCTCAAACGGAATTTTGGCCAACCACATCCAGAAGGCTACCGAAAGGCACTGCGGTTOATGAAACAGGC
TGAGAAATTTGGCCGTCAGTTGTGACCTTTATCAATACAGCAGGTGCTTATCCTGGTGTCGGAGCGGAA
OACGTTGGTCAAGGGGAAGCTATCGCTCGCAATCTCATGGAATGAGTGACCTGAAAGTTCCTATTATCG
CCATTATTATCGGTGAAGGTGGTTCAGGCGGGGCTCTGGCTCTAGCTGTGCGGGACCGTGTCTGGATGCT
CGAAAATTCTATCTATGCCATTCTCAGTCCAGAAGGCTTTGCTTCCATTTTATGGAAGGACGGTACTCGCG
CCATGGAAGCAGCAGAACTGATGAAAATCACTTCGCATGAACTGTTAGAAATGGACGTGGTGGATAAGG
TGATTTCTGAAGTAGGACTTTCTAGTAAAGAACTAATTAAGAGTGTCAAAAAAGAACTCCAAACGGAGCT
GGCTAGACTTTTCAAAAAACCGCTAGAAGAGTTGCTGGAAGAACGCTATCAACGATTTAGAAAATACCT
CGAGCACCACCACCACCACCTGA

2 CFE75 "homologue of SEQ. ID NO. 71"

Fig 93
ATGTCAGATAAGATTGGCTTATTACAGGCTCATTGATCCGATGACAAATGGGCATCTGGATATCATTG
AACGGGCGAGCAGACTTTTGTATAAGCTTTATGTGGGTATTTTTTTAATCCCAACAACAAGGATTTCTT
CCTATCGAAAATCGTAAACGGGGGCTAGAAAAGGCTTTGGGACATCTGGAATAATGTTGAAGTCGTGGCT
TCTCATGATGAATTGGTGGTTCGATGTTGCAAAAAGATTGGGTGCTACTTGTCTAGTGGCTGGTTTGAGGA
ATGCGTGGGATTGCAATATGAAGCCAGTTTGTATTACTACAATCATCAGCTGTCTTCTGATATAGAGACT
ATTTATTACATAGTCGACCTGAACATCTCTATATCAGTTTCATCAGGCGTTAGAGAGCTTTTGAAGTTTGG
TCAGGATATTGCCGTGCTATGTTCCCGAGAGTATTTGGAGGAAAGCGGCGCACTCGAGCACCACCACCAC
CACCACCTGA

2 CFE76 "homologue of SEQ. ID NO. 72"

Fig 94
ATGACGATTTTGTGTTGTGGTTATCAGTGCTTCTTTCTGTATATGGTTTCTCTTAGCATGAAACCCTATCAA
ACAGCTAAAAGTGAAGGAGAAAAATTAGCTCAGCAGTATGCAGGATTAGAGCAGGCTGATCAGGTTGAT
TTATACAATGGCTTGAATCTTATTACAGCGTTCTTGGTTCGTAAATAACAGCAAGAAGCGCTTGCTGTCT
GATTGGTAAAGATGACCATAAGATTACGTTTATCAGCTAAATCAGGGTATTTTACAAGAAAAAGCAGA
AACGGTTTCTAAGGAAAAGGGAGCTGGCGAGATTGACAAGATAACCTTTGGTTCGTTATCAAGACAAGCC
AATCTGGGTAGTTAAGTCAGGATCTGATTTTATCTAGTAGATTTTGAAACAGGAGCATTGGTCAACAAG
GAGGGCTACTCGAGCACCACCACCACCACCTGA

2 CFE78 "homologue of SEQ. ID NO. 74"

Fig 95
ATGTTTACAATCGATAAAGAAAAATTTCAGTTTGTAAAACGTGACGATTTTGCCTCTGAAACTATTGATG
CGCCAGGATATTCTTACTGGAAATCAGTGTTTAAACAATTTATGAAGAAAAAATCAACTGTAGTCATGTT
GGGAATCTTGGTAGCCATCATTTTGATAAGTTTCATCTACCCAATGTTTTCTAAGTTTGATTTCATGATG
TCAGCAAGGTAAACGACTTTAGTGTTCTGTTATATCAAGCCAAATGCGGAGCATTGGTTCGGTACTGACAG
TAACGGTAAATCGCTCTTTGACGGTGTCTGGTTCGGAGCTCGTAACCTCCATCCTCATTTCTGTGATTGCCA
CAGTGATTAACCTTGGTTATCGGTGTTTTTGTGCGGTGGTATTTGGGGTATTTCAAAATCAGTTGACCGTGTC
ATGATGCAAGTTTACAACGTCTCTCAAACATCCACCTCTTTTGATTGTTATTGTCTTGACTTACTCAAT
CGGAGCTGGATTCTGGAATCTGATTTTGGCCATGAGCGTAACAACATGGATTGGTATTGCCTTCATGATCC
GTGTGCAAAATCTTGGCTATCGTGACTTGGAATACAACCTTGGCGTCACGTACTTTGGGAACACCAACCTT
GAAGATTOTTGCCAAAAATATCATGCCTCAATTGGTATCTGTTATTGTGACAACCATGACTCAAAATGCTTC
CAAGCTTTATCTCATACGAAGCCTTCTTGTCTTTCTTCCGGTCTTGGATTACCGATTACAGTGCCAAGTTTG
GGTCTGTTGATTTCCGATTATTCACAAAACGTAACAACCAATGCTTACTTGTCTGGAATTCATTGACAAC

2 CFE 78 (Contd)

CCCTTGCTTGGTATCCTTGTCCCTTTTCGTAGTTGGTCAAACTTAGCGGATGCTAGTGATCCACGTACAC
ATAGACTCGAGCACCACCACCACCACCCTGA

2 CFE 79 "homologue of SEQ. ID NO. 75"

ATGTATAACCTATTATTAACCATTTTATTAGTATTATCTGTTGTGATTGTGATTGCAATTTTCATGCAACCA
ACCAAAAACCAATCCAGCAATGTATTTGATGCCAGTTCAGGTGATTGTTTGAACGCAGTAAAGCTCGCG
CTTTTGAAGCTGTAATGCAGCGTTTGACAGGGATTTTAGTCTTTTCTGGCTAGCCATTGCCTTAGCATTG
ACGGTATTATCAAGTAGACTCGAGCACCACCACCACCACCCTGA

2 CFE 80 "homologue of SEQ. ID NO. 76"

ATGTTTCTGAGAAATAAATTATTTTTTGGACCACAGAAATTTTACTCTTAACCATCATCTTTTACCTATGG
AGACAGATGGGATCTTTGATTAACCCCTTTTGTAGCGTGCTTAATAACAATTATGATTCCATTTTATTAGG
GGCTTTCTTTATTATTGACAAACCCTATTGTTACTTTCTTAAATAAAGTCTGTAAACTCAATCGTTTGCT
TGGTATTTAATTACCTTGTGTACTTTGGTCTGGGGAATGGTCATAGGTGTTGTCTATCTCTTACCTATTTT
GATTAATCAGTTATCTAGTTTGATTATATCTAGTCAAACCTATTTATAGTCGAGTACAAGACTTAATCATAG
ACTTATCTAATTATCCTGCGCTCCAGAATTTGGATGTAGAAGCTACAATTCAGCAGTTAAACTTATCCTAT
GTGATATTCTTCAAAATATCCTAAATAGCGTATCAAATAGTGTGGGGAGCGTCTTGTGAGCTCTTATCAG
TACTGTTTGTATTGATTATGACTCCAGTTTTTTTTGGTTTATTTCTTATTAGATGGACATAAATTCTTGCC
ATGCTTCAAAAGAACGATTCTAAAGAGGGATCGCTTGCATATTGCAGGCTTATTAAAGAATTTAAATGCGA
CGATTGCTCGGTATATTAGTGGAGTTTCGATTGACGCAATCATTATAGGTTGTTTGGCTTATATTGGCTAT
AGTATTATTGGTTTAAATATGCTTTAGTTTTTGCCATTTTTTCTGGTGTAGCCAATTTAATTCCTTATGTG
GGCCAAGTATTGGTTTGAATTCCTATGATCATCGCAAATATATTCACTGATCCCCATAGACTGCTGATTGC
AGTGATTTATATGCTTGTGTTTCAGCAGGTAGATGGCAATATCTTATATCCTCGAATTGTAGGAAGTGTTA
TGAAGGTCATCCAATCACGATTTTAGTTTTACTTTTGTGTCAGCAATATCTATGGTGTAGTTGGAATG
ATTGTCCAGTGCCAACCAATCTATCTTGAAAGAAATTTCTAAGTTCTTATCCCCTTTGTATGAAATCA
TAAATAATGAAGAAGAGAGAAAGAGAATTAGCTAAGCTCGAGCACCACCACCACCACCCTGA

2 CFE 81 "homologue of SEQ. ID NO. 77"

ATGTATCAAGGACTTTATCGAAAATATAGAAGTCAAAACTTCTCCAGTTAGTTGGTCAAGAAGTTGTGG
CTAAGACTCTTAAACAAGCGGTGGAGCAAGAGAAATAAGTCACGCTTATCTTTTTTCTGGTCCTCGTGG
AAGGGGAAAAACAGTGTGCTAAATCTTTGCCAAGGCTATGAACGTGCCAATCAAGTGGGTGGCGA
ACCTTGCATAACTGCTATATTTGTCAAGCAGTGACGGACGGTAGTTTGAAGATGTCATTGAAATGOAT
GCAGCTTCTAATAATGGGGTAGATGAAATTCGCGAAATTCGTGATAAATCTACCTATGCGCCTAGCCTTG
CTGTTATAAGGTTTATATCATAGATGAGGTTTACATGCTGTCTACAGGGGGCTTTTAAATGCCCTCTTAAAG
ACCTGTGAAGAACCAACACAGAATGTAGTCTTTATTTTGGCCACTACTGAATTGCCACAAGATTCTGTCTA
CTATTCTATCCCGTGTGCAACGTTTTGAGTTTAAATCAATTAAGACACAGGATATTAAGGAACATATTAC
TATATCTTAGAATAAGAAATATCAGTTCTGAACCAGAGGCTGTGGAAATCATTGCCAGACGGGGCGGAA
GOTGGAATGCGGGACGCTTGTCTATTTTGGATCAAGCCCTGAGTTTGACACAGGGGAAATGAGGTGACGA
CTGCTATCTCTGAAGAAATTAAGTGGCACCATTAGCCTACCAGCCTTGGATGATTATGTGGCGGCTTGTCT
CAACAGGATGTTCCCAAAGCTTTGTCTTGTCTTGAATCTTCTTTTGAACAATGGTAAGAGCATGACTCGTTT
TGTGACCGATCTTTTGCATATTTAAGAGACTTGTAAATTTGTTCAAAACAGGGGGAGAAATACTCATCAT
AGTTTCACTCTTTGTAGAAAATTTGGCACTTCTCAAAAAAATCTGTTTGAATGATTTCGCTTAGCAACAGT
GACTTTAGCAGATATTAAGTCTAGTTTGCAGCCCAAGATTTATGCTGAAATGATGACCGTCCGTTTGGCG
GAAATCAAGTCCGAACCAGCTCTATCAGGAGCGGTTGAAATGAAATGCTACGCTGAGACAGGAAGTT
GCCGCTTCAAAACAGAGCTTTCTAATGTAGGTGCGGTTCTTAAACAAGTTGCAACCAGCTCCTAGTCCGAC
CAGCTACGGGCAAAACAGTCTATCGTGTGATCGCAATAAAGTGCAATCTATCTTACAAGAGGCCGTCGA
AAATCCTGATTAGCAGGTCAAATTTAATTCGTTTGCAGAATGCCTGGGGAGAGGTAATTGAAAGTCTA
GGTGGGGCGGACAAGCTCTGCTCGAGCACCACCACCACCACCCTGA

2 CFE 82 "homologue of SEQ. ID NO. 78"

ATGTTTCGATTACCAATAAGTTAGCGGTATCGAACTTGATTAAAAACCGCAAACTCTACTATCCTTTTGC
GCTGGCTGTTCTTGGCAGTCACTGTACCTATCTCTTTTACTCTCTAACCTTCAATCCTAAGATTGCGGA
AATCCGTGGAGGAACAACCATTCAGGCTACACTTGGATTGTTGTTGTCGTCACCTTGGCGTCAGCC
ATTATCGTTCTCTATGCCAATAGTTTTGTCATGAAGAACCGTTCCAAGGAAGTGAATTTATGGCATGTT
GGGCTTGGAGAAGCGTCATCTTATCAGTATGACCTTTAAGGAGTTAGTGGTATTGGGATTCTAACTGTTG
GAGCGGTATCGGTATTGGAGCCTTGTGTTGACAAGTTAATTTTCGCTTCTGCTCAAAGTAATGAAATTG

2 CFE 85 (contd)

AGCCCAAGTGGATATTGAAGCGATTAGTGAAACGACTGTTGTCAAAGCAAATCAACAGGTTAGTAAAAGG
CGTTCCGAAAAAATCAATGATTTGAACGAGCCTGTGAAGACGGTTAGTGAAGAAACCGTTGACCTTGGT
CATGTGGTTGATGCTATTAATAAATAAGAGGAAGAAGGTCAAGGTATTTCTGATGAAGTCAAGGCTGAA
ATCTTAAACATGAAGACATGCCAGCACTATCTTAGAAGAAACTGGTCACATTGAGATTTTAAATGAAC
TTCAAATCGAGGAAGCGATGAGGGAAGAAGCAGGCGCTGATGACCTTGAAACTGAGCAAGACCAAGCTG
AAAGTCAAGAACTAGAAGACTTGGGCTTGAAAGTTGAAACGAACTTTGATATTGAACAAGTAGCTACGG
AAGTAATGGCTTATGTTCAAACGATTATTGATGACATGGATGTTGAGGCTACACTTTCAAATGATTATAA
CCGTCTGATGATCAATCTACAAATTGACACCAACGAACCAGGTCGTATTATCGGCTACCATGGTAAAGTC
TTGAAGGCCTTGCAACTGTTGGCTCAAATTTATCTTTACAACCGCTATTCCAGAACCTTCTACGTTACAAT
CAATGTCAATGATTATGTGCAACACCGTGCAGAAGTCTTGCAGACCTATGCGCAAAAATTGGCGACTCGT
GTTTGGAAAGAAGGGCGCAGTCATAAAACAGATCCAATGTCAAATAGCGAACGCAAGATTATCCATCGT
ATTATTACAGTATGGATGGCGTGACTAGTTACTCTGAAGGTGATGAGCCAAATCGCTATGTTGTTGTAG
ATACAGAACTGGAGCACCACCACCACCACCCTGA

2 CFE 86 "homologue of SEQ. ID NO. 82"

ATGTCAATTTTCCATTATTTTAGCAGCGGGTAAAGGGACTCGCATGAAATCTGATTTGCCAAAAGTTTT
GCACAAGGTTGCGGGTATTTCTATGTTGGAACATGTTTCCGTAGTGTGGGAGCTATCCAACCTGAAAAG
ACAGTAACAGTTGTAGGACACAAGGCAGAATTGGTTGAGGAGGTCTTGGCTGAACAGACAGAATTTGTG
ACTCAATCTGAACAGTTGGGAAGTGGTCATGCAGTTATGATGACAGAGCCTATCTTAGAAGGTTTGTGAG
GACACACCTTGGTCATTGCAGGAGATACTCCTTTAATCACTGGTGAAAGCTTGAAAACTTGATTGATTT
CCATATCAATGATAAAAATGTGGCCACTATCTTGACTGCTGAAACGGATAATCCTTTTGGCTATGGACGA
ATTGTTGTAATGACAATGCTGAGGTTCTTCGTATTGTTGAGCAGAAGGATGCTACAGATTTTGAAAAGC
AAATCAAGGAATCAACACTGGAACATACGTCTTTGACAACGAGCGTTTGTGTTGAGGCTTTGAAAAATAT
CAATACCAATAACGCTCAAGGCGAATACTATATTACAGACGTCATTGGTATTTTCCGTGAAACTGGTGAA
AAAGTTGGCGTTTATACTTTGAAAGATTTTGATGAAAGTCTTGGGGTAAATGACCGTGTGGCGCTTGCCA
CAGCTGAGTCAGTTATGCGTCGTCGCATCAATCATAAACACATGGTCAACGGTGTTAGCTTTGTCAATCC
AGAAGCAACTTATATCGATATTGATGTTGAGATTGCTCCGGAAGTTCAAATCGAAGCCAATGTTATCTTG
AAAGGGCAAACGAAAATTGGTGCTGAGACTGTTTGGACAAACGGTACTTATGTAGTGGACAGCACTATC
GGAGCAGGAGCGGTCAATTACCAATTCTATGATTGAGGAAGTAGTGTGTCAGACGGTGTGACAGTCCGT
CCTATGCTCACATTGCTCCAAATTCAAGTCTGGGTGCCCAAGTTCAATTTGGTAACTTTGTTGAGGTGAA
AGGATCTTCAATCCGTGAGAATACCAAGGCTGGTCATTTGACTTATATCGGAAACTGTGAAGTGGGAAGC
AAGGTTAATTTGGGTGCTGGAACCTATTACAGTCAACTATGACGGCAAAAACAAATACAAGACAGTCATTG
GAGACAATGTCTTTGTTGGTTCAAATTCAACCATTATTGCACCAGTAGAACTTGGTGACAATTCCTCGTT
GGTGCTGTTGTAACCTATTACTAAAGACGTGCCAGCAGATGCTATTGCTATTGGTCCGGTCTCAGATCA
ATAAAGACGAATATGCAACACGTCTTCCTCATCATCCTAAGAACCAGCTCGAGCACCACCACCACCACCA
CTGA

2 CFE 87 "homologue of SEQ. ID NO. 83"

ATGTCCAAGATTCTAGTATTTGGTCACCAAAATCCAGACTCAGATGCCATCGGGTCACTCTGTAGCTTTTGC
CTACCTTGCAAAGAAGCTTACGGTTTGGATACGGAAGCTGTTGCCCTTGGAACCTCAAATGAAGAAACA
GCCTTTGTCTTGAACCTATTTTGGTGTGGAAGCACCACGTGTTATCACTTCTGCCAAAGCAGAGGGGGCAG
AGCAAGTTATCTTGAAGTACCACAATGAATTCACAACATCTGTATCAGATATCGCTGAAGTAGAAGTTTA
CGCTGTGTAGACCACCACCGTGTGGCTAACCTTTGAAACTGCAAGCCCACTTTACATGCGTTTGGAGCCA
GTTGGAACAGCGTCTTCAATCGTTTACCGTATGTTCAAAGAACATGGTGTAGCTGTGCCCTAAAGAGATTG
CAGGTTTATGCTTTTCAAGGTTTGAATTTTCAAGATACCGTTCTTTTGAATCACCAACAACACACCCAAACAGAT
AAAATCATTTGCTCCTGAATTGGCTGAATTGGCTGGTGTAAACTTGGGAAGAATATGGTTTGGCAATGTTGA
AAGCTGTACCAACTTGGCTAGCAAATCTGCTGAAGAATTGATTGACATCGATGCTAAGACTTTTGAAGT
CAACGGAAATAATGTCCGTGTTGCCCAAGTGAACACAGTTGACATCGCTGAAGTTTGGGAACGCCAAGCA
GAAATTGAAGCTGCAATGCAAGCTGCCAACGAATCAAACGGCTACTCTGACTTTGTCTTGATGATTACAG
ATATCGTCAACTCAAACTCAGAAATATTGGCTCTTGGTGCCAATATGGACAAGGTGGAAGCGGCTTTCAA
TTTCAAACCTTGAAAACAATCATGCCTTCCTTGGTGGTGCCGTTTACGTAAGAAACAAGTGGTACCTCAAT
TAATGAAAGCTTTAATACGCTCGAGCACCACCACCACCACCCTGA

2 CFE 88 "homologue of SEQ. ID NO. 84"

ATGATTTCAAAGAGATTAGAATTGGTAGCTTCTTTGTGTACAGGGGGCTATTTTACTAGATGTGGGAA
GTGACCATGCTTATCTGCCTATCGAGTTGGTTGAGAGAGGCCAAATCAAAGCGCTATTGCAGGTGAGGT

2CFE 88 (contd)

GGTGAAGGTCCCTATCAGTCTGCGGTTAAAAATGTTGAGGCTCACGGCCTAAAGGAGAAAATCCAAGT
 CCGTTTAGCCAATGGCTTGGCAGCTTTTGAAGAGACTGACCAAGTGTCTGTCTATTACCATTTGCTGGCATG
 GGTGGTGGTTTGATTGCTAGGATTTTAGAAGAAGGTTTGGGGAAGTTAGCTAATGTADAGCGTTTGATCC
 TCCAGCCCAATAATCGTGAAGACGACTTGCGTATCTGGCTACAGGATCATGGATTCCAGATTGTAGCAGA
 AAGAATCTTAGAAGAAGCTGGAAAGTTTTATGAGATTTTGGTGGTGGAAAGCAGGACAAATGAAGCTATC
 AGCCAGTGATGTTGCTTTGGTCCCTTCTTGTCCAAAGAAGTCAGTCCAGTATTTGTCCAAAAATGGCAA
 AAAGAAGCTGAGAAGCTAGAGTTCCGCCCTCGGACAAATCCCAGAAAAAATCTGGAAGAAGCTCAAGTT
 CTAGTAGATAAGATTCAAGCTATCAAGGAGGTGCTCCATGTTAGCAAGCTCGAGCACCACCACCACC
 ACTGA

2 CFE89 "homologue of SEQ. ID NO. 85"

ATGAATTTAAACGATATTAAAGACTTGATGACTCAATTTGACCAGTCAAGTTTGAGAGAATTTTCTTATA
 AAAATGGGACGGATGAGTTGCAGTTTAGCAAGAATGAAGCAAGACCTGTGCCTGAAGTTGCAACTCAAG
 TCGCTCCAGCACCCGTTCTAGCAACACCGAGTCCAGTAGCTCCTACATCTGCTCCAGCAGAGACTGTAGC
 AGAAGAAGTTCCAGCTCCAGCTGAAGCAAGTGTGGCTACTGAGGGAAATCTTGTAGAGAGTCCACTTGT
 GGAGTGGTTTACTTGGCTGCTGGACCAGATAAACCTGCCTTCGTTACAGTTGGTGATAGTGTCAAAAAAG
 GTCAAAACATTGGTAATTATCGAAGCCATGAAAGTCATGAATGAATCCCAGCTCCTAAGGATGGTGTGGT
 AACGGAAATTCTCGTCTCTAACGAAGAAATGGTTGAGTTTGGTAAAGGATTGGTACGTATCAAACTCGAG
 AACCAACCACCACCACCCTGA

2 CFE90 "homologue of SEQ. ID NO. 86"

ATCAAACTAAATCGAGTAGTGGTAACAGGTTATGGAGTAACATCTCCAATCGGAAATACACCAGAAGAA
 TTTTGGAAATAGTTTAGCAACTGGGAAAATCGGCATTGGTGGCATTACAAAATTTGATCATAGTGACTTTG
 ATCTGCATAATGCGGCAGAAATCCAAGATTTTCCGTTTCGATAAATACTTTGTAAAAAAGATACCAACCG
 TTTTGATAACTATTCTTTATATGCCCTTGATGCAGCCCAAGAGGGCTGTAAACCATGCCAATCTTGATGTAG
 AGGCTCTTAATAGGGATCGTTTTGGTGTTATCGTTGCATCTGGTATTGGTGGAAATCAAGGAAATTGAAGA
 TCAGGTACTTCGCCCTTCATGAAAAAGGACCCAAACGCTGTCAAACCAATGACTCTTCCAAAAGCTTTACCA
 AATAATGGCTTCTCGGAATGTAGCCATGCGTTTTGGTGCAAACGGTGTTTGTAAATCTATCAATACTGCCTG
 CTCTTCAACAAATGATGCGATTGGGGATGCCCTTCGCTCCATTAAAGTTTGGTTTCCAAGATGTGATGTTGG
 TGGGAGGAACAGAAGCTTCTATCACACCTTTTGCCATCGCTGGTTTCCAAGCCTTAACAGCTCTCTCTACT
 ACAGAGGATCCAACTCGTGCTTCGATCCCATTTGATAAGGATCGCAATGGGTTTGTATGGGTGAAGGTT
 CAGGGATGTTGGTTCTAGAAAGTCTTGAACACGCTGAAAAACGTGGAGCTACTATCCTGGCTGAAGTGOT
 TGGTTACGGAAATACTTGTGATGCCTACCACATGACTTCTCCACATCCAGAAGGTCAGGGAGCTATCAAG
 GCCATCAAACTAGCCTTGGAAGAAGCTGAGATTTCTCCAGAGCAAGTAGCCTATGTTAATGCTCACGGAA
 CGTCAACTCCTGCCAATGAAAAAGGAGAAAGTGGTGCTATCGTAGCTGTTCTTGGTAAGGAAGTACCTGT
 ATCATCAACCAAGTCTTTTACAGGACATTTGCTGGGGGCTGCGGGTGCAAGTGAAGTATCAGATTATATCGAAGCTA
 GAAGCTATGCGTCATAACTTTGTACCAATGACAGCTGGGACAAGTGAAGTATCAGATTATATCGAAGCTA
 ATGTCGTTTATGGACAAGGTTTGGAGAAAGAAATTCCATACGCTATTTCAAATACTTTTGGTTTGGAGGC
 CACAATGCAGTTCTTGCTTTCAAACGTTGGGAGAAATAGACTCGAGCACCACCACCACCACCCTGA

2 CFE91 "homologue of SEQ. ID NO. 87"

ATGAACATCTATGATCAACTACAAGCTGTAGAAGACCGTTATGAAGAAGTAGGAGAATTGCTGAGTGAC
 CCTGATGTGCTTTCAGACACCAAGCGTTTTATGGAGCTTTCAAAGAAGAAGCTTCCAATCGTGACACCG
 TAATAGCCTACCGTGAGTATAACAAGTCTTCAAATATCGTCGATGCCGAAGAGATGATTAAGGAATC
 AGCCCGAGATGCGGACTTGGAAGAAATGGCCAAGCAAGAACTCAAAGATGCCAAGGCTGAAAAAGAAG
 AATATGAAGAAAACTGAAAAATTTGCTCCTTCCAAGGATCCAACCGATGACAAGAATATCATCCTTGA
 AATCCGTGGAGCAAGCTGGTGGAGACGAAGCGGCACTTTTCGCTGGAGATTGCTAACTATGTACCAAAAG
 TATGCGGAAGCCCAAGGTTGGCGCTTTGAAGTCATGGAAGCCTCTATGAATGGTGTGGTGGTTTAAAG
 AAGTGGTTGCTATGGTTTCAAGGTCAAGTCTGTATACTCTAAGCTTAAGTATGAATCAGGTGCCACCGTGTG
 CAACGTGTTCTGTGACAGAAAGCCAAGGCCGTGTTCACTTTCGACAGCGACAGTTCTTGTATGCCAG
 AAGTTGAAGAGGTTGAATACGACATTGATCCAAAAGACCTTCGTGTGACATCTATCACGCCTCTGGTGC
 TGGTGGACAGAACGTCAATAAGGTTGCGACTGCCGTTTCGTATCGTTCACTTGCCAACCAATATCAAGGTT
 GAGATGCAGGAAGAAGCTACCCAGCAGAAGAACCAGGAGAGGCTATGAAGATTATCCGTGCACGCGTC
 GCTGACCCTTTGCTCAGATTGCTCAGGATGAAGAAGACGCTGAGCGTAAGTGCACAATCGGTACTGGTG
 ACCGTTCAAGACGGATCCGAACCTTATAACTTCCCACAAAACCGTGTACAGACCACCGTATCGGCTTGAC

(contd.)

Fig 108

2CFE91 (contd.)

CCTCCAAAACTAGATACGATTTTGTCTGGTAAATTGGACGAAGTTGTGGATGCCTTGGTGCTTTATGACC
AAACACAAAACTAGAAGAATTAAACAAACTCGAGCACCACCACCACCACCCTGA

2CFE92, "homologue of SEQ. ID NO. 88"

ATGGCCTACACTCTTAAACCTGAAGAAGTCGGCGTTTTTGCCATCGGTGGTCTAGGAGAAATCGGGAAAA
ACACTTACGGAATTGAATACCAAGACGAGATTATCATCGTCGATGCTGGGATTAAATTCCCAGAAAGATGA
CTTGCTTGGTATCGACTATGTCAATTCCTGACTACTCTTACATCGTAGACAATATCGACCGCGTCAAGGCTG
TTTAAATCACACACGGACACGAGGACCACATTGGTGGGATTCCGTTCTACTCAAGCAAGCAAATGTCCC
TATTTATGCTGGACCGCTTGCCTTGGCTTTGATCCGTGGGAAACTCGAAGAACACGGCCTCTTGCGCAAC
GCCAACTTTACGAAATCAACCACAAACACCGAGTTGACCTTTAAAAATCTCAAGGCAACTTTCTTTAGAA
CGACTCACTCTATTCCAGAGCCTTTGGGGATTGTCAATTCATACTCCTCAAGGGAAAAATCGTCTGTACGGGT
GACTTTAAGTTCGACTTTACTCCAGTTGGAGAACCTGCGGACTTGCATCGTATGGCTGCGCTTGGTGAAG
AAGGCGTGCTCTGTCTCTGTCTGACTCGACAAATGCGGAAGTACCAACCTTTACCAACTCTGAAAAAGT
CGTGGTTCAGTCCATTATGAAGATTATCCAAGGTATTGAAGGACGTATCATCTTTGCATCCTTTGCCTCAA
ATATCTTCCGTCTCCAGCAGGCAACAGAAGCTGCTGTTAAGACTGGACGCAAGATTGCGGTCTTTGGTCC
TTCTATCGAAAAGGCCATTGTCAACGGAATCGATCTTGGCTACATCAAAGCTCCTAAGGGAACTTTATC
GAOCCAAATGAATCAAAGATTATCCTGCAGGAGAAGTTCTTATCCTCTGTACAGGTAGTCAGGGTGAGC
CTATGGCAGCCCTCTCTCGTATCGCCAACGGAACCCACCGTCAAGTACAATTACAACCAGGTGATACCGT
TATCTTCTCTCTAGTCCCATCCCTGGAAACACTACTAGCGTCAACAAGCTGATTAAACATCATTTCTGAAG
CTGGTCTCGAAGTTATCCACGGTAAAGTGAACAATATCCATACATCTGGACACGGTGGCCAGCAAGAGC
AAAAACTCATGCTCCGCTTGATTAAAGCCAAAAATACTTCATGCCGTGTCACGGTGAATACCGCATGCAAAA
AGTCCACGCTGGACTAGCAGTGGATACTGGTGTGTGAAGGACAATATCTTTATCATGAGCAATGGCGAT
GTGCTTCCCTTACTGCTGACTCAGCTCGTATCGCAGGTCAATTCACGCCCAAGATATCTATGTGATGG
AAATCGTATCGGTGAAATTGGCGCAGCTGTCTCAAAGATCGTCCGATCTATCTGAAGACGGTGTCTGT
CTAGCAGTCGCAACTGTTGACTTCAAATCGCAGATGATTCTGTCTGGCCAGATATCCTCAGCCGAGGCT
TTGTCTACATGAGAGAGTCTGGAGACTTGATTTCGCCAAAGCCAGCGTATCCTCTTCAATGCCATTCTGATC
GCACTGAAAAATAAGGATGCTAGCGTGCAATCTGTCAA
TCTATGAAAAATACCGAACGTGAACCGATCATCATCCCG/
CCACCACCACCACCTGA

Fig 109

2CFE94

ATGGCTACGGCAACAAAAAAGAAAAAATCAACAGTTA/
AAGGCCAAGACGATTGAAAAATATCTAGGCAGAACTACAAGGTTTTAGCCAGTGTGGGTCATATCCGT
GATTTGAAGAAATCCAGTATGTCCGTGATATTGAAAAATAATTATGAACCGCAATATATTAATATCCGAG
GAAAGGCCCTCTTATCAATGACTTGAAAAAAGAAGCTAAAAAAGCTAATAAAGTTTTTCTCGCGAGTG
ACCGCGACCGTGAAGGAGAAGCGATTTCTTGGCATTGCGCCATATTCTCAACTTGGATGAAAAATGATGC
CAACCGTGTGGTCTTCAATGAAATCACCAAGGATGCAATCAAAAATGCTTTTAAAGAACCTCGTAAGATC
GATATGCACTTGGTGGATGCCCAACAAGCTCGTGGATCTTGGATCGCTTGGTAGGGTATTTCGATTTCTGC
CTATTTTGTGGAAGAAGGTCAAGAAGGGCTTGTCAAGCAGGTGCGGTTCACTCCATTGCCCTTAAACTCAT
CATTGACCGTGAAAAATGAAATCAATGCCTTCCAGCCAGAAGAATACTGGACAGTTGATGCTGTCTTTAAA
AAGGGAACCAACAATTTCAATGCTTCTTCTATGGAGTAGATGGTAAAAAGATGAAACTGACCAGCAAT
AAGGAAGTCAAGGAAGTCTTGTCTCGTCTGACGAGTAAAGACTTTTCAGTAGATCAGGTGGATAAGAAA
GAGCGTAAGCGCAATGCTCCTTTACCCTATACCACTTCATCTATGCAGATGGATGCTGCCAATAAAATCA
ATTTCCGTACTCGAAAAACCATGATGGTTGCCCAACAGCTCTATGAAGGAATTAATATCGGTTCTGGTGT
TCAAGGTTTGATTACCTATATGCGTACCGATTGACTCGTATCAGTCCGTGATGCGCAAAATGAGGCGGCA
AGGTTTCAATACCGATCGTTTTGGTAGCAAGTATTCTAAGCACGGTAGCAAGGTCAAAAACGCATCAGGTG
CTCAGGATGCCCATGAGGCTATTCTGTCCTCAAGTGTCTTTAATACACCAGAAAGCATCGCTAAGTATCT
GGACAAGGATCAGCTCAAGCTATATACCTTATCTGGAATCGTTTTGTGGCTAGCCAGATGACAGCGGCC
GTTTTTGATACCAATGGCTGTTAAATTGTCTCAAAAAGGGGTTCAATTTGCTGCCAATGGTAGTCAGGTAA
GTTTGATGGTATCTTGGCATTATATAATGATTCTGACAAGAATAAGATGTTACCGGACATGGTTGTTGGAG
ATGTGGTCAAAACAGGTCAATAGCAAACCAGAGCAACATTTACCCAACCGCCTGCCCGTTATTCTGAAGC
AACACTGATTAACCTTAGAGGAAAATGGGGTTGGACGTCCATCAACCTACGCGCCAACCATTTGAAAC
CATTCAGAAACCTTATTATGTTCCGCTGGCAGCCAAACGTTTTGAACCGACAGAGTTGGGAGAAAATTGTC
AATAAGGTCATGTTGAATATTTCCAGATATCGTAAACGTGACCTTCACAGCTGAAATGGAAGGTAAAC
TGGATGATGTCGAAGTCGGAAAAGAGCAGTGGCGACGGGTCAATTGATGCCTTTTACAAACCATTTCTCTAA

Fig 110

2 CFE 94 (cont'd)

Fig 110 (cont'd)

AGAAGTTGCCAAGGCTGAAGAAGAAATGGAAAAAATCCAGATTAAGGATGAACCAGCTGGATTTOACTG
TGAAGTGTGTGGTAGTCCAATGGTCATTAACTTGGTCGTTTTGGTAAATTCTACGCTTGTAGCAATTTCC
CAGATTGCCATCATAACCAAGCAATCGTGAAAGAGATTGGTGTGAGTGTCCAAGCTGTCATCAGGGACA
AATTATTGAGCGAAAAACCAAGCGTAATCGCCTATTCTATGGTTGCAATCGCTATCCAGAATGTGAATTT
ACCTCTTGGGACAAGCCTGTTGGTCGTGACTGTCCAAAATGTGGCAACTTCCACATGGAGAAAAAAGTCC
GTGGTGGTGGCAAGCAGGTTGTTGTAGCAAAGGCGACTACGAGGAAGAAAAGATGGCTCTTTGTCAACT
GCTCGAGCACCACCACCACCACCCTGA

2 CFE95 "homologue of SEQ. ID NO. 91"

ATGTTTATTTTCATCAGTGCTGGAATTGTGACATTTTACTAATTTAGTAGGAATTCGGGCTTTATCCA
ATTTATAGAAAGGCGCAAATTACAGGCCAGCAGATGCATGAGGATGTCAAACAGCATCAGGCAAAAGC
TGGGACTCCTACAATGGGAGGTTTGGTTTTCTTGATTACTTCTGTTTTGGTTGCTTTCTTTTCGCCCTATT
AGTAGCCAATTTCAGCAATAATGTGGGAATGATTTTGTTCATCTTGGTCTTGTATGGCTTGGTCGGATTTT
AGATGACTTTCTCAAGGTCTTTCGTAAAATCAATGAGGGGCTTAATCCTAAGCAAAAATTAGCTCTTCAG
CTCTAGGTGGAGTTATCTTCTATCTTTCTATGAGCGCGGTGGCGATATCCTGTCTGTCTTTGGTTATCCA
GTTCATTTGGGATTTTCTATATTTTCTTCGCTCTTTTCTGGCTAGTCGGTTTTTCAAACGCAGTAAACTTG
ACAGACGGTGTGACGGTTTAGCTAGTATTTCCGTTGTGATTAGTTTGTITGCCTATGGAGTTATTGCCTA
TGTGCAAGGTGAGATGGATATTCTTCTAGTGATTCTTGCCATGATTGGTGGTTTGTCTCGGTTTCTTCATCTT
TAACCATTAAGCCTGCCAAGGTCTTTATGGGTGATGTGGGAAGTTTGGCCCTAGGTGGGATGCTGGCAGCT
ATCTCTATGGCTCTCCACCAGGAATGGACTCTCTTGATTATCGGAATTGTGTATGTTTTTGAACAACCTTC
TGTATGATGCAAGTCAGTTATTTCAAACCTGACAGGTGGTAAACGTATTTTCCGTATGACGCTGTACATC
ACCATTTTGAGCTTGGGGGATTGTCTGGTAAAGGAAATCCTTGGAGCGAGTGAAGGTTGACTTCTTCTT
TTGGGGAGTTGGTCTTCTAGCAAGTCTCCTGACCCTAGCAATTTTATATTTGATGCTCGAGCACCACCACC
ACCACCCTGA

Fig 111

2 CFE96 "homologue of SEQ. ID NO. 92"

ATGGCAGCGGAATTTTCACTTGAAAAAACTCGTAATATCGGTATCATGGCTCACGTGATGCCGGTAAAA
CAACAACCTACTGAGCGTATTCTTTACTACACTGGTAAATCCACAAAATCGGTGAAACTCACGAAGGTGC
GTACAAATGGACTGGATGGAGCAAGAGCAAGAACGTGGTATCACGATCACATCTGCTGCCACAACAGC
TCAATGCAACAACACCGCGTAAACATCATCGACACACCAGGACACGTGGACTTCACAATCGAAGTACA
ACGTTCTCTTCGTGTATTGGATGGTGGGTTACCGTTCTTGACTCACAATCAGGTGTTGAGCCTCAAACCTG
AAACAGTTTGGCGTCAAGCAACTGAGTACGGAGTTCCACGTATCGTATTTGCCAACAATAATGGACAAAAT
CGGTGCTGACTTCTTTACTCTGTAAAGCACACTTCACGATCGTCTTCAAGCAAAATGCACACCCAATCCAAT
TCCCAATCGGTCTGTAAGATGACTTCCGTGGTATCATTGACTTGATCAAGATGAAAGCTGAAATCTATAC
TAACGACCTTGGTACGGATATCCTTGAAGAAGACATCCCAGCTGAATACCTTGACCAAGCTCAAGAATAC
CGTGAAAAATGATTGAAGCAGTTGCTGAAACTGACGAAGAATTGATGATGAAATACCTCGAAGGTGAA
GAAATCACTAACGAAGAATTGAAAGCTGGTATCCGTAAAGCGACTATCAACGTTGAATTCTTCCGAGTAT
TGTGTGTTTCAGCCTTCAAAAACAAAGGTGTTCAATTGATGCTTGATGCGGTTATCGACTACCTTCCAAGT
CCACTTGACATCCCAGCAATCAAAGGTATTAACCCAGATACAGACGCTGAAGAAATTCGTCCAGCATCTG
ACGAAGAGCCATTTCAGCTCTTGCCTTCAAGATCATGACTGACCCATTCTGAGGTGCTTTGACATTCTTC
CGTGTTTACTCAGGTGTTCTTCAATCAGGTTTACATCGTATTGAATACTTCTAAAGGTAAACGTGAACGTAT
CGACGTTATCCTTCAAATGCACGCTAACAGCCGTCAAGAAATCGACACTGTTTACTCAGGTGATATCGCT
GCTGGCGTTGGTTTGAAGATACTACAACCTGGTGACTCATTGACAGATGAAAAAGCTAAAATCATCCTTG
AGTCAATCAAGCTTCCAGAACCAGTTATCCAATTGATGGTTGAGCCAAAATCTAAAGCTGACCAAGACAA
GATGGGTATCGCCCTTCAAAAATTTGGCTGAAGAAGATCCAACATTCCGCGTTGAAACAAACGTTGAAACT
GGTGAACAGTTATCTCAGGTATGGGTGAACCTTACCTTGACGTCCTTGTGATCGTATGCGTCGTGAGTT
CAAAGTTGAAGCGAAGCTAGGTGCTCCTCAAGTATCTTACCGTGAAACATTCCGCGCTTCTACTCAAGCA
CGCGGATTTCTTCAAACGTCAGTCTGGTGGTAAAGGTCAATTCCGGTGATGTATGGATTGAATTTACTCAA
ACGAAGAAGGTAAAGGATTTCGAATTCGAAAACGCAATCGTCCGGTGGTGTGGTTCCCTCGTGAATTTATCCC
AGCGGTGAAAGAGGTTTGGTAGAATCTATGGCTAACGGTGTCTTTCAGGTTACCCAATGGTTGACGTT
AAAGCTAAGCTTTATGATGGTTTATATCAGGATGTGCACTCATCTGAAACTGCCTTCAAGATTGCGGCTTC
ACTTCCCTTAAAGAAGCTGCTAAATCAGCACAACCAGCTATCCTTGAACCAATGATGCTTGTAACAATC
ACTGTTCCAGAAGAAAACCTTGGTGATGTTATGGGTACGTAACCTGCTCGTGGACGTGTAGATGGTA
TGGAAGCACACGGTAACAGCCAAATCGTTCTGTGCTTACGTTCCACTTGGTGAAATGTTTCGGTTACGCAAC
AGTTCTTCTGCTTCTGCATCTCAAGGACGTGGTACATTGATGATTGACCCTACGAAGATGTACCTA

Fig 112

2CFE 96 (contd.)

AGTCAGTACAAGAGAAATTATTAAGAAAAATAAAGGTGAAGACCTCGAGCACCACCACCACCACCTG

2CFE97 "homologue of SEQ. ID NO. 93"

ATGCCAAATTACAATATTCATTTCACCGCCTGATATCACAGAAGCAGAAATTGCTGAAGTAGCGGATA
CCCTGCGTTCTGGTTGGATCACACAGGTCCTAAAACAAAAGAACTGGAGCGCCGCTTGCTCTTTACAC
ACAGACACCTAAGACTGTTTGTCTCAACTCTGCGACAGCCGCTCTGGAGTTGATTTACGCGTTTTOGAAO
TGGGAOCTGGTGATGAAGTCATCGTTCCAGCCATGACCTATACGGCTTCATGTAAGTGTACATTACGCACGT
GGGAGCAACCCCTGTCATGGTGGATATCCAAGCAGATACGTTTGAGATGGACTATGACCTGCTTGAGCAA
GCTATCACTGAGAAAATAAGGTGATTATCCCAGTAGAGCTCGCAGGGATTGTTTGGCATTATGACCGTT
TGTTCCAAGTCTGGAGAAAAACGTGACTTCTTTACCGCTTCAAGCAAGTGGCAAAAGGCCTTTAACCG
TATTGTCATTGTCTCTGATAGTGCCACGCTTTGGGATCTACTTATAAAGGACAACCTTCTGGTTCTATCG
CTGATTTTACTTCTCTCATTCATGCTGTTAAGAAGCTTTACAACGGCAGAAGGTGGAAGTGGGACTTGG
AAAGCCAATCCAGTGATTGATGACGAAGAGATGTACAAGGAATCCAAATCCTTTCCCTTCACGGGCAAA
CTAAGGATGCTCTTGCCAAGATGCAACTGGGGTCATGGGAATACGATATCGTTACACCAGCCTATAAGTG
CAACATGACCGATATCATGGCTTCACCTTGGTTTGGTACAATTGGACCGCTATCCAAGTTTGTGCAACGCC
GTAAGGACATTGTGGACCGCTATGATAGTGGTTTTCAGGTTCTCGCATCCATCCTTTGGCACACAAGAC
TGAAACTGTGCAATCTTCACGCCACCTCTACATCACCCGTGTAGAAGGAGTAAGECTAGAAGAACGCAAC
CTCATCATCCAAGAATTGGCTAAAGCAGGAATTGCAAGTAATGTTCACTACAAACCGCTTCTCTCTGA
CAGCCTATAAGAATCTTGGATTTOATATGACCAACTATCCTAAGGCCTATGCCTTCTTTGAGAATGAAATT
ACCTCCTCTTTCATACTAAATTAAGCGATGAAGAAGTAGACTATATCATTGAGACTTTCAAAACAGTTT
CTGAAAAAGTCTAATTTATCAAAAAAACTCGAGCACCACCACCACCACCTG

2CFE99 "homologue of SEQ. ID NO. 95"

ATGTTTATACTTATTTGCGTGGATTAGTTGTATTGCTCTTATGGTCCATCAATGGCAATGCTCACTATCAT
AATACTGATAAAATTCCTAATCAAGATGAAAATTATATTTTAGTTGCGCCTCACCGTACCTGGTGGGATC
CTGTTTATATGGCCTTTGGCACCAGCCAAAACAGTTTCATCTTATGGCAAAAAAAGAACTCTTTACCAA
CCGTATCTTTGGTTGGTGGATTTCGTATGTGTGGCGCCTTTCCCATCGACCGTGAAAATCCCAGCGCCTCAG
CCATCAAAATATCCTATCAACGTTCTCAAAAAAAGTGACCGCTCTCTCATCATGTTTCCAAGTGGTAGCCGC
CACTCAAAACGATGTCAAGGGGGGGCGCAGCACTGATTGGCAAAATGGCCAAGGTCCGTATCATGCCGGTT
ACCTAGACCGGTCCCATGACTTTGAAGGGCTTGATTAGCCGTGAACGTGTGATATGAACCTTTGGAAATC
CAATCGATATCTCAGATATCAAGAAAATGAATGATGAAGGCATTGAAACAGTCGCCAATCGTATTCAAA
CAGAATTCCAACGTCTGGACGAAGAAACGAAACAATGGCACAATGATAAAAAACCAAAATCACTCTGGT
GGTTTATCCGCATCCCTGCCCTCATCCTTGCTATTATCCTCGCTATCCTAACCATCATCTTTAGCTTTATCG
CAAGCTTCATCTGGAACCCAGATAAGAAAAGAGAAAGAACTTGCACTCGAGCACCACCACCACCACCT
GA

2CFE101 "homologue of SEQ. ID NO. 97"

ATCACCAACGAATTTTACATTTTGAAAAAATCAGCCGCCAGACTTGGCAATCTTTACATCGAAAGACAA
CACTCCTTTGACAGAAGAAGAAATTGGAATCTATCAAGAGTTTAAATGACCAAATCAGTCTCCAAGACGT
TACAGATATCTATCTCCCTTGGCTCATCTGATTGAGATTACAAGCGAACTAAGGAAGATTAGCCTTTT
CAAAAGGAATTTCTCTCAACGTGAAAGTAAATCTCAACCTTTTATTATTGGGGTTTCTGGGAGTGTTGCC
GTGGGAAATOCACAACCAGTCGCTACTTCAAATCCTACTGTCCCGTACGTTTACAGATGCTACGGTTG
AGTTGGTTACAACCTGATGGTTTCTCTATCCCAATCAAACCTTGATTGAGCAGGGGATTTTAAATCGTAAA
GGATTTCTGAAAGCTATGATATGGAAGCTCTTCTCAACTTCTTGGACCGCATCAAAAATGGACAAGATG
TAGATATTCCTGTCTATTCTCATGAAGTTTACGACATCGTACCCGAAGAGAAACAAAGTGTCAAAGCTGC
TGATTTTGTAAATGTTGAGGGAATCAATGTCTTTCAAAATCCACAAAACGATCGTCTCTATATCACTGACT
TCTTTGACTTTTCCATCTATGTAGATGCTGGAGTGGATGATATTGAAAGTTGGTATCTGGACCGTTTCTTG
AAAATGCTGAGTCTAGCCCAAAACGACCCCTGATAGCTACTATTATCGTTTACTCAGATGCCGATTGGGG
AAGTGGAAAGCCTTTGCCCATCAGGTCTGGACCAATATCAATCTCACAAATCTACAAAATTATATTGAACC
AACCAGAAATCGTGCAGAAGTGATTCTTCATAAAAGCAAGAACCATGAAATCGATGAAATTTACTTAA
AAAGCTCGAGCACCACCACCACCACCTGA

2CFE102 "homologue of SEQ. ID NO. 98"

ATGGAAATTTCAATTATTAACAGATGTTGGTCAGAAACGAACAAATAACCAAGACTATGTCAACCACTATG
TCAATAGAGCTGGACGTACCATGATTATTTAGCTGATGGGATGGGAGGTTCATCGCGCAGGGAATATCGC

2 CFE 102 (contd.)

Fig 116 (contd.)

TAGTGAAATGGCGGTACAGACCTGGGTGTAGCTTGGGTGATACCCAGATCGATACAGTCAATGAAGTG
CGTGAATGGTTCGCCCATTAACCTAGAAATTGAAAATCAAAAGATTACCCAGCTTGGTCAGGATGAAGCTT
ACAGAGGCATGGGAACACTTTTGGAAAGTCCTTGCTATTATTGATAATCAGGCTATCTATGCTCATATTGGT
GATTCGCGTATCGGCTTGATTCTGTGGAGAAGAATACCATCAGTTGACGAGCGATCATTCTTGGTTAATG
AATTGCTCAAGGCTGGTCAATTGACACCAGAAGAGGCGAGAAGCTCATCCGCAAAAAAATATTATCAACC
AGTCTATTGGGCAAAAAGATGAAATTCAGCCTGATTTTGGGACAGTTATCCTTGAGTCAGGTGACTATCT
CTTGCTCAATAGTGACGGCTTGACCAACATGATTTTCAGGCAGTGAGATTCTGTGATATTGTAACCAAGTGAT
ATTCTTTAGCAGATAAAACGGAGACACTTGTTCGTTTTGCTAACAATGCAGGAGGTTTAGACAACATTA
CGGTTGCCCTTGTTCCTATGAACGAGGAGGATGAAGAACTCGAGCACCACCACCACCACCTGA

Fig 117

2 CFE103 "homologue of SEQ. ID NO. 99"

ATGACGATACAGATGAAGAATACAGGTAAACGAATTGATCTGATAGCCAATAGAAAACCGCAGAGTCAA
AGGGTTTGTATGAATTGCGAGATCGTTTGAAGAGAAATCAGTTTATACTCAATGATACCAATCCGGATA
TTGTCATTTCCATTGGCGGGGATGGTATGCTCTTGTCCGGCCTTTCATAAGTACGAAAAATCAGCTTGACAAG
GTCCGCTTATCGGTCTTCATACTGGACATTTGGGGCTTCTATACAGATTATCGTGATTTTGAGTTGGACAA
GCTAGTGACTAATTTGCAACTAGATACTGGGGCAAGGGTTTCTTACCCTGTTCTGAATGTGAAGGTCTTTC
TTGAAAATGGTGAAGTTAAGATTTTCAGAGCACTCAACGAAGCCAGCATCCGACGGTCTGATCGAACCAT
GGTGGGAGATATTGTAATAAATGGTGTTCCTTTGAACGTTTTCTGTGGAGACGGGCTAACAGTTTCGACA
CCGACTGGTAGTACTGCCTATAACAAGTCTCTTGGCGGTGCTGTTTTACACCCTACCATTGAAGCTTTGCA
ATTAACGGAGATTGCCAGCCTTAATAATCGTGTCTATCGAACATTGGGGCTCTTCCATTATTGTGCCTAAGA
AGGATAAGATTGAACCTATTCCAAACAAGAAACGATTATCATACTATTTCCGTTGACAATAGCGTTTATTCT
TTCCGTAATATTGAGCGTATTGAGTATCAAATCGACCATCATAAGATTCACTTTGTCCGAGCTCCTAGCCA
TACCAGTTCTGGAACCGTGTTAAGGATGCCTTTATCGGTGAGGTGGATGAACTCGAGCACCACCACCAC
CACCACCTGA

Fig 118

2 CFE104 "homologue of SEQ. ID NO. 100"

ATGTCAAAGAAATTAATTTTCATCAGATGCCCGTTCAGCCATGGTTCTGTGGTGTGATATCCTTGCAAG
ACACTGTAAAGTAACCTTGGGACCAAAAGGTCGCAATGTCTGTTCTTGAAAAGTCATTCCGTTACCCCTT
GATTACCAATGACGGTGTGACCATTGCCAAAGAAATCGAATTGGAAGACCATTTTGAAAATATGGGTGCT
AAGTTAGTATCAGAAGTAGCTTCTAAAACCAATGATATCGCAGGTGACGGGACTACGACTGCAACAGTCT
TGACCCAAAGCTATCGTCCGTGAAGGAATCAAAAACGTCACAGCAGGTGCAAAATCCAATCCGTATTCTGTCG
TGGGATTGAAACAGCAGTTGCCGCGCAGCAGTCGAAGCTTTGAAAACAACGCCATCCCTGTTCCCAATAA
AGAAGCTATCGCTCAAGTTGCAGCCGTATCTTCTCGTTCTGAAAAGTTGGTGAAGTACATCTCTGAAGCA
ATGGAAAAGTTGGCAAAGACGGTGTATCACCATCGAAGAGTCAAGTGGTATGGAAACAGAGCTTGAA
GTGGTAGAAGGAATGCAGTTTGACCGTGGTTACCTTTACAGTACATGGTGAAGTATAGCGAAAAAATGG
TGCGTGAACCTTGAAAATCCGTACATTTTGATTACAGACAAGAAAATTTCCAATATCCAAGAAATCTTGCC
ACTTTTGAAAGCATTTCTCCAAAGCAATCGTCCACTCTTGATTATTGCGGATGATGTGGATGGCGAGGCT
CTTCCAACCTCTTGTTTTGAACAAGATTCTGTGGAACCTTCAACGTAGTAGCAGTCAAGGCACCTGGTTTGG
TGACCGTTCGCAAAGCCATGCTTGAAAGATATCGCCATCTTAACAGGCGGAACAGTTATCACAGAAGACCTT
GGTCTTGAGTTGAAAGATGCGACAATTGAAGCTCTTGGTCAAGCAGCGAGAGTGACCGTGGACAAAGAT
AGCAGCGTTATTGTAGAAGGTGCAGGAAATCCTGAAGCGATTCTCACCGTGTGCGGTTATCAAGTCTC
AAATCGAAACTACAACCTTCTGAATTTGACCGTGAAAAATTGCAAGAACGCTTGGCCAAATTGTGAGGTGG
TGTAGCGGTTATTAAAGGTGGAGCCGCAACTGAAACTGAGTTGAAAGAAATGAAACTCCGCATTGAAGA
TGCCCTCAACGCTACTCGTGCAGCTGTTGAAGAAGGTATTGTTGCAGGTGGTGGAAACAGCTCTTGCCAAT
GTGATTGACAGCTGTTGCTACCTTGGAATTGACAGGAGATGAAGCAACAGGACGTAATATTGTTCTCCGTG
CTTGGGAAGAACCCGTTCTGTCAAATTGCTCACAATGCAGGATTGGAAGGATCTATCGTTATCGATCGTTTG
AAAAATGCTGAGCTTGGTATAGGATTTAACGCAGCAACTGGCGAGTGGGTAAACATGATTAATCAAGGT
ATCATTTGATCCAGTTAAAGTGAGTCGTTTCAGCCCTACAAAATGCAGCATCTGTAGCCAGCTTGATTTTGA
CAACAGAGCAGTCGTAGCCAATAAACCAGAACCAGTAGCCCCAGCTCCAGCAATGGATCCAAGTATGA
TGGGGGGGATGATGCTCGAGCACCACCACCACCACCTGA

Fig 119

2 CFE105 "homologue of SEQ. ID NO. 101"

ATGATTAAGATTGAAACCGTATTAGATATTTTAAAGAAAGATGGCCTTTTTTCGCGAAATTATTGACCAAG
GTCATTACCACTACAACCTACAGCAAAGTTATTTTGTATAGCATCAGCTACGACAGCCGAAAAGTAACAGA
AGACACTCTTTTGTGAAAAGGCGCTGCCTTTAAAAAAGAATACCTTCTTTCTGCTATAACACAAGGTT
TAGCTTGGTATGTAGCTGAAAAGGACTACGAAGTCGATATCCCTGTCTCATTTGTGAACGATATAAAGAA

2 CFE 105 homologue of SEQ ID NO: 101 (Contd)

AGCCATGAGTTTGATTGCCATGGAGTTCTATGGTAATCCACAAGAGAACTCAAACCTTGCCTTTACT
 GGTACTAAGGGTAAGACAACAGCAACCTATTTTCGCCTATAACATCTTATCTCAAGGGCATAGACCTGCTA
 TGTGTGACCATGAACACAACCTCTTGATGGCGAGACTTTCTTTAAGTCAGCGTTGACAACCCCTGAGAG
 TATTGACCTCTTTGACATGATGAATCAGGCTGTGCAAAATGACCGTACCCACCTCATCATGGAAGTCTCC
 AGTCAAGCCTATCTAOTCCATCGAGTCTATGGACTGACCTTTGATGTAGGAGTCTTTCTTAACATCACTCC
 TGACCATATCGGCCCCGATTGAACACCCTAGCTTTGAAGACTATTTCTACCACAAGCGTCTCTTGATGGAA
 AATAGCCGAGCAGTCATCATTAAACAGTGACATGGACCACTTCTCAGTCTTGAAAGAAGAGGTTGAAGATC
 AAGACCATGATTTCTATGGTAGCCAATTTGATAACCAAATCGAGAATTCCAAAGCCTTTAGCTTTTCAGGT
 ACGGGTAAACTCGCTGGAGATTATGATATCCAACCTCATTGGCAACTTCAACCAAGAAAATGCAGTTGCTG
 CTGGACTGCTTGTCTCCGTCTCGAGCAAGTCTTGAGGACATCAAAAAAGGCATCGCTGCAACCCGCGT
 TCGTGGTCTGATGGAAAGTCTCACTCAGAAAAATGGAGCCAAGGTCTTCATCGACTATGCCCACAATGGG
 GATAGTCTGAAAAAACTCATCAATGTGGTTGAAACTCATCAAAACCGGAAAGATTGCTCTGGTTCTGGGAT
 CAACAGGAAAACAAGGGAGAAAGTCGTCTGAAGGACTTTGGCCTCCTCCTCAATCAACACCCTGAGATTC
 AAGTCTTCTGACTGCTGATGACCCTAACTATGAAGACCCAATGGCCATTGCAGATGAAATTAGTAGCTA
 CATCAATCATCCTGTTGAAAAGATTGCGGATCGCCAAGAAGCCATCAAGGCGGCAATGGCTATCACAAA
 TCACGAATTAGATGCAGTTATTATTGCGGGTAAGGGAGCCGATTGTTACCAAATCATCCAGGGCAAGAAA
 GAATPCTACCCAGGAGATACAGCCGTCGCAGAAAATTATTACTCGAGCACCACCACCACCACCTGA

2 CFE106 "homologue of SEQ. ID NO. 102"

ATGATCCAAATCGGCAAGATTTTTCGCGGACGCTATCGGATTGTCAAACAGATTGGTTCGAGGAGGCATGG
 CGGATGTCTACCTAGCCAAAGACTTAATCTTAGATGGGGAAGAAGTGGCAGTGAAGGTTCTGAGGACCA
 ACTACCAGACCGGACCCGATAGCTGTAGCTCGTTTTTCAGCGTGAAGCGAGAGCTATGGCAGATCTAGACCA
 TCCTGATATCGTTTCGGATAACAGATATTGGTGAGGAAGACGGTCAACAGTATCTTGCAATGGAGTATGTT
 GCTGGACTAGACCTCAAACGCTATATCAAGGAACATTATCCTCTTTCTAATGAAGAAGCAGTCCGTATCA
 TGGGACAAATTCTCTTGCTATGCGCTTGGCCCATACTCGAGGAATTGTTTACAGGGGACTTGAAACCTCA
 AAATATCCTTTTGACACCAGATGGGACTGCCAAGGTCAAGACTTTGGGATTGCTGTAGCCTTTGCAGAG
 ACAAGTCTGACCCAGACTAACTCGATGTTGGGCTCAGTTTCACTTGTCAACAGAGCAGGCGCGTGGTT
 CGAAGGCGACTGTGCAGAGTGATATCTATGCCATGGGGATTATTTTCTATGAGATGTTGACAGGCCATAT
 CCTTATGACGGGGATAGCGCGGTGACCAATTGCCCTCCAGCATTTCCAGAACCCCTGCCGTCCGTTATTO
 CAGAAAATTCACTGTACCTCAGGCTTTAGAAAATGTTATTATCAAGGCAACTGCTAAAAAGKTOACCAA
 TGGCTATCGCTCGGTTTCAGAGATGTATGTAGACTTGTCTAGTAGCTTGTCTCTACAATCGTAGAAAATGAAA
 GTAAGTTAATCTTTGATGAAACGAGCAAGGCAGATACCAAGACCTTGCCGAAGGTTTCTCAGAGTACCTT
 GACATCTATTCTTAAGGTTCAAGCGCAGACAGAACACAAATCAATAAAACCCCAAGCCAGGCTGTGAC
 AGAGGAACCTTACCAACCACAAGCACCGAAAAAACATAGATTAAAGATGCGTTACCTGATTTTGTGGCC
 AGCCTTGTATTGGTGGCAGCTTCTCTTATTTGGATACTATCCAGAACTCCTGCAACCATTGCCATTCCAGA
 TGTGGCAGGTCAGACAGTTGCAGAGGCCAAGGCAACGCTCAAAAAAGCCAATTTTGAGATTGGTGAGGA
 GAAGACAGAGGCTAGTGAAAAGGTGGAAGAAGGGCGGATTATCCGTACAGATCCTGGCGCTGGAACCTGG
 TCGAAAAGAAGGAACGAAAATTAATCTGGTTGTCTCATCAGGCAACAATCCTTCCAAATTAGTAATTAT
 GTGGGCGGGAATCTTCTGATGTTATCGCGGAATTAAGAGAAAAAGTTCCAGATAATTTGATTAAAA
 TTGAGGAAGAAGAGTCGAATGAAAGTGAGGCTGGAACGGTCTGAAGCAAAGTCTACCAGAAGGTACG
 ACCTATGACTTGAAGCAAGGCAACTCAAATTGTTTTGACAGTAGCTAAAAAGCTACGACGATTCAATTAG
 GGAACCTATATTGGACGGAACCTCTACAGAAGTAATCTCAGAACTCAAGCAGAAGAAGGTTCTGAGAATT
 TGATTAAAGATAGAGGAAGAAGAGTCCAGCGAAAGCGAACCAGGAACGATTATGAAACAAAGTCCAGGT
 GCGGGAACGACTTATGATGTGAGTAAACCTACTCAAATTGTCTTGACAGTAGCTAAAAAGTTACAAGTG
 TTGCCATGCCGAGTTACATTGGTTCCAGCTTGGAGTTTACTAAGAACAATTTGATTCAAATTGTTGGGATT
 AAGGAACCTAATATAGAAGTTGTAGAAGTGACGACAGCGCTGCAGGTAGTGTAGAAGGCATGGTTGTT
 GAACAAAGTCTAGAGCAGGTGAAAAGGTAGACCTAAATAAGACTAGAGTCAAGATTTCATCTACAAA
 CCTAAAACAACCTCAGCTACTCCTGCGGCCGCACTCGAGCACCACCACCACCACCTGA

2 CFE107 "homologue of SEQ. ID NO. 103"

ATGAAAGATTTTGATACTATTTGTCATCGGTGGGGGACCTGCTGGTATGATGGCTACGATTTCCAGTAGCTT
 TTATGGACAGAAAACCCCTCCTCATCGAAAAAATCGGAAACTTGGAAAAAATTAGCTGGGACTGGTGG
 GGGACGTTGCAATGTGACCAACAATGGTAGCTTAGACAACCTGCTAGCTGGAATTCCTGGAAACGGACG
 CTTCTTTACAGTGTTTTCTCCAGTTCGATAATCATGACATCATCAACTTTTTTACAGAAAATGGTGTTAA
 ACTTAAGGTGCAAGACCACGGACGCGTCTTCCAGCCAGTGACAAGTCTCGGACTATTATCGAAGCTTTG
 GAAAAGAAAATCACTGAACCTAGGTGGTCAAGTTGCTACTCAAATAGAAAATCGTTTCTGTTAAAAAGTA

2CFE 107 (contd)

Fig 121 (contd)

GATGACCAGTTTGTCTTAAGTCAACGGATCAAACCTTCACTTGTAAGAACTCATTGTGACAAACAGGTG
GTAAGTCTTATCCTTCGACTGGTTCGACTGGCTTTGGTCACGAGATTGCTCGCCATTTTAAGCATACCATC
ACCGATCTTGAGGGCTGCTGAAAGTCTTTATTAACAGATTTTCCACATAAAGCCTTACAAGGGATTCTCT
GGACGATGTGACCCTAAGTTATGGTAAGCATGTCATCACTCATGATTTACTCTTTACCCACTTTTGGTTTGT
CAGGTCTGCTGCCCTACGCATGTCTAGCTTTGTCAAAGGTGGGGAGGTCTCTCACTCGATGTTTTGCCT
CAACTTCTGAGAAGGACTTGGTTACATTTCTAGAAGAAAATCGGGAAAAATCCTTGAAAAACGCTTTAA
AAACCTTGTTACCAGAACGCTTGGCCGAATTTTTTGTACAAGGATATCCTGAAAAAGTCAAACAGCTGAC
TGAAAAGGAACGAGAACAACCTTGTCAGTCCATTAAAGAACTTAAAATTCCTGTAAGTGGAAAAATGTC
CCTTGCAAAGTCTTTGTTACCAAGGGTGGAGTCAGTCTCAAGGAAATCAATCCTAAAACCTTGAAAGT
AAGCTGGTACCTGGCCTCCACTTTGCAGGCGAAGTTATGGATATCAATGCCACACGGGTGGCTTTAACA
TCACTTCTGCCCTCTGTACCGGCTGGGTGGCGGGAAGTCTGCATTATGATCTCGAGCACCACCACCA
CCTGA

Fig 122

2 CFE108 "homologue of SEQ. ID NO. 104"

ATGCTGAAATGGGAAGACTTGCCTGTGGAAATGAAATCAAGCGAGGTGAGTCTTACTACCAGCTTGTCT
CTAAAAGGAAGGGTTCGCTGATTTTCAAGCGTTGCTTGGACTGGGTTTGGCCTTGGTCTTACTGGTTCTA
ACTTCTCCCATCTTTCTCATCTTGAGCATTGAGATCAAGTTGGATAGCAAGGGGCCAGTGATTTACAAGCA
AGAGCGTGTGACCCAGTACAACCGTCGGTTCAAGATTGGAAGTTCGGTACCATGGTGACGGATGCGGAT
AAAAAAGGAAGTCTGGTGACTTCTGCTAACGATAGCCGTATTACCAAGGTTGGAAATTTTATCCOACGTG
TCCGTTTGGACGAAGTGCCTCAATTGGTCAATGTCCTTAAAGGTGAGATGTCTTTGTGCGGTACACGACCT
GAAGTGCCACGTTATACAGAGCAGTATAGCCCTGAAATGATGGCAACCTTGCTCTTGCAAGCAGGAATTA
CCTCTCCAGCCAGCATCAACTACAAGGATGAGGACACCATCATCAGTCAAATGACGGAGAAAGGTCTGT
CAOTTGATCAGGCCTATGTGGAGCATGTTCTTCTGAAAAGATGCGCTATAACCTCGCCTATCTCCGAGA
GTTTAGTTCTTTGGGGACATCAAAATCATGTTTCAAACCGTGTTTGAGGTACTAAAACCTCGAGCACCACC
ACCACGACCACTGA

Fig 123

2 CFE109 "homologue of SEQ. ID NO. 105"

ATGACTAGTCCACTATTAGAATCTAGACGCCAACTCGGTAAATGCGCTTTTCAAGCTCTCATGAGCCTTGA
GTTCCGTACGGATGTGGAAGTCTTGTGCTTTCGCCTATACTCATGATCGTGAAGATACGGATGTACAA
CTTCCAGCCTTTTGTATAGACCTCGTTTCTGGTGTTCAGCTAAAAGGAAGAACTAGATAAGCAAATCA
CTCAGCATTTAAAAGCAGGTTGGACCATTTGAACGCTTAAACGCTCGTGGAGAGAAACCTCCTTCGCTTGGG
AGTCTTTGAAATCACTTCAATTGACACTCCTCAGCTGGTTGCTGTTAATGAAGCTATCGAGCTTGCAAAGG
ACTCTCCGATCAAAAATCTGCCCGTTTATCAATGGACTGCTCAGCCAGTTTGTAAACAGAAGAACAAC
CGAGCACCACCACCACCACCACTGA

Fig 124

2 CFE111 "homologue of SEQ. ID NO. 107"

ATGAGAAAACGTGTAACGATTATTGATGTAAAAGACTATGTTGGTCAAGGAAGTGACGATTGGCGCTTGGG
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2 CFE112 "homologue of SEQ. ID NO. 108"

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2 CFE113 "homologue of SEQ. ID NO. 109"

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2 CFE114 "homologue of SEQ. ID NO. 110"

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2 CFE115 "homologue of SEQ. ID NO. 111"

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2CFE 115 (contd)

Fig 128 (contd)

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 CACCACGA ||

Fig 129

2 CFE116 "homologue of SEQ. ID NO. 112"

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2 CFE 116 (contd)

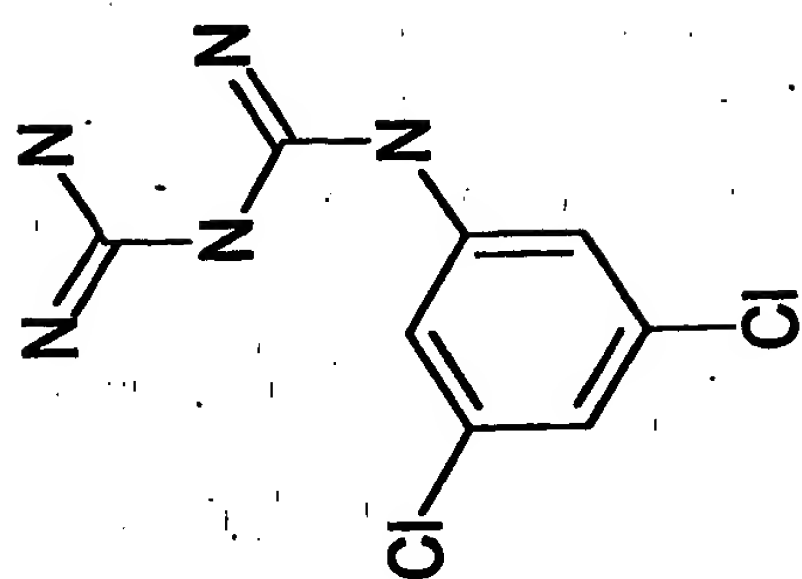
Fig 129
(contd)

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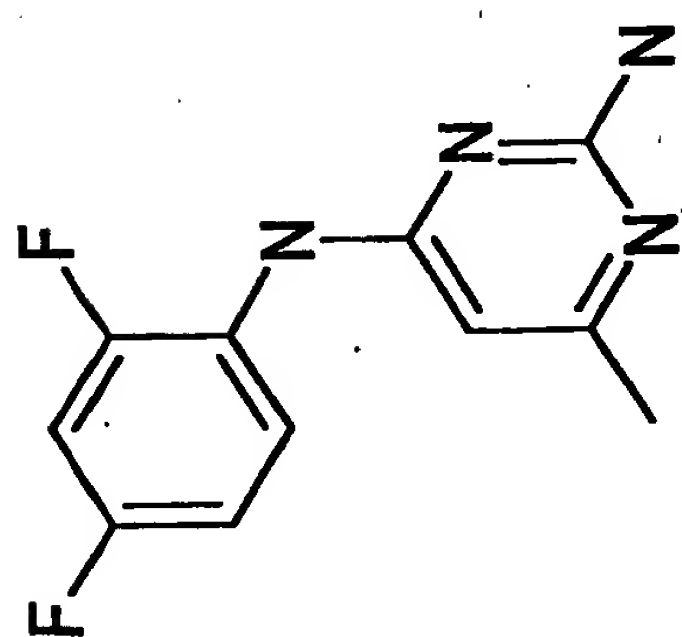
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Fig 130

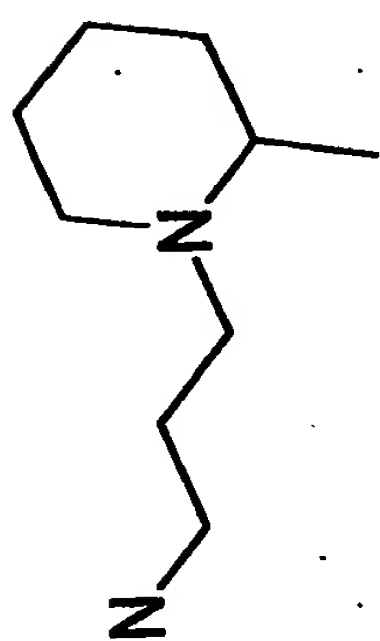
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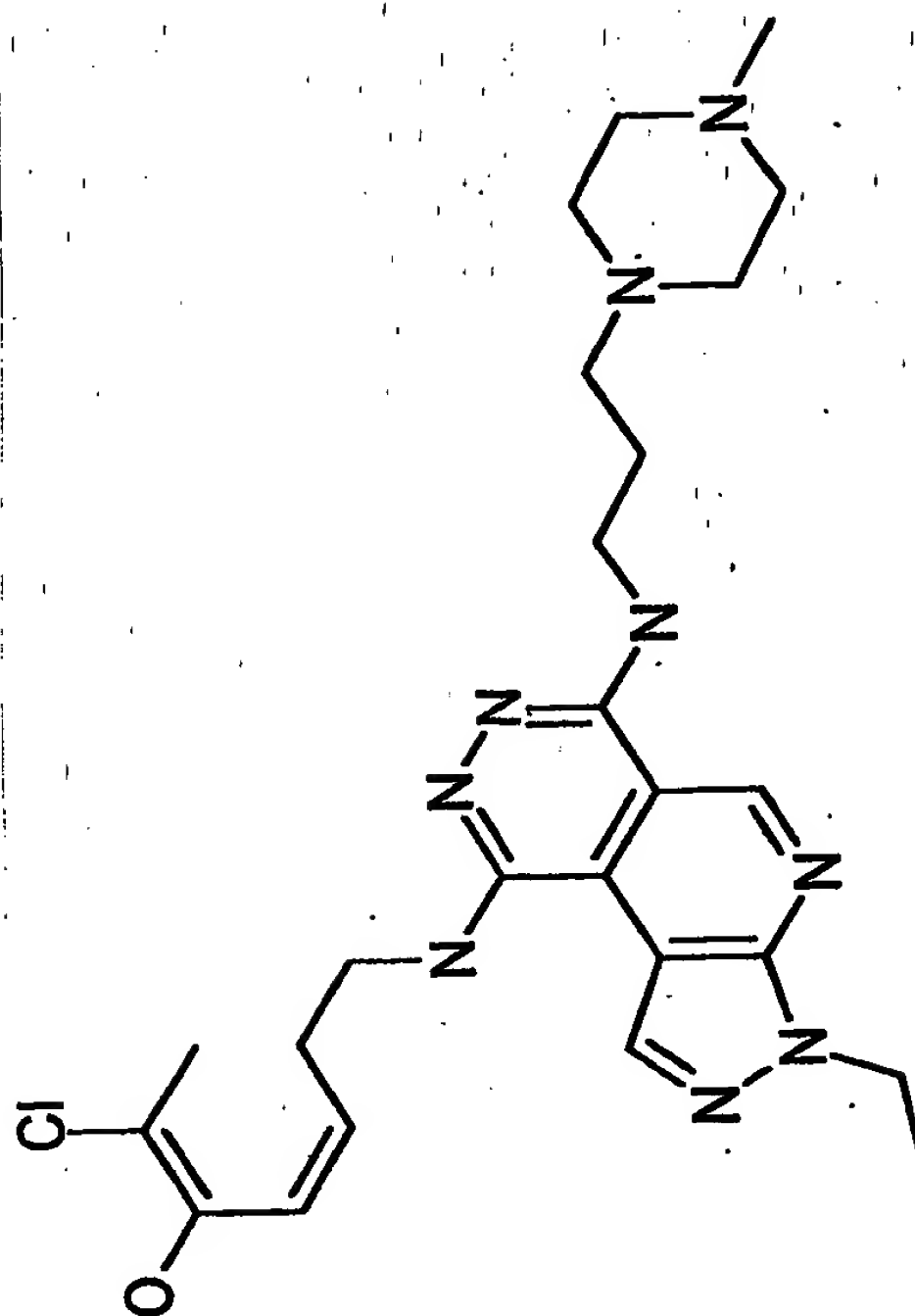
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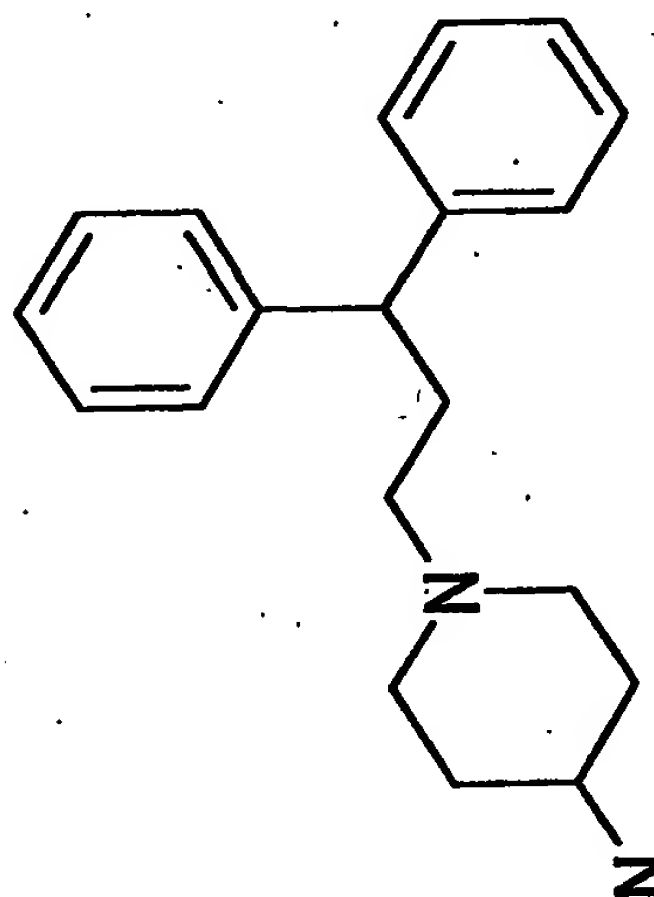
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A



E



D

FIGURE 131

SEQUENCE LISTING

5 <110> Dougherty, Thomas J.
 Pucci, Michael J.
 Dougherty, Brian A.
 Davison, Daniel B.
 Bruccoleri, Robert E.
 Thanassi, Jane A.

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 FOR CELL VIABILITY AND THEIR USES

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<211> 852

<212> DNA

<213> Streptococcus pneumoniae

55

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<213> Streptococcus pneumoniae

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<211> 1023

15 <212> DNA

<213> Streptococcus pneumoniae

<400> 11

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<210> 12

<211> 1344

40 <212> DNA

<213> Streptococcus pneumoniae

<400> 12

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<210> 13

<211> 783

<212> DNA

<213> Streptococcus pneumoniae

15

<400> 13

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<210> 14

<211> 276

<212> DNA

<213> Streptococcus pneumoniae

35

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<211> 840

<212> DNA

<213> Streptococcus pneumoniae

45

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<211> 930

10 <212> DNA

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<211> 1662

<212> DNA

<213> Streptococcus pneumoniae

35

<400> 17

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<212> DNA

<213> Streptococcus pneumoniae

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<211> 519

30 <212> DNA

<213> Streptococcus pneumoniae

<400> 21

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<210> 22

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<212> DNA

<213> Streptococcus pneumoniae

<400> 22

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<210> 23

<211> 561

<212> DNA

<213> Streptococcus pneumoniae

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<210> 24

<211> 1572

<212> DNA

<213> Streptococcus pneumoniae

<400> 24

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<211> 846

<212> DNA

<213> Streptococcus pneumoniae

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<210> 26

<211> 1290

<212> DNA

25 <213> Streptococcus pneumoniae

<400> 26

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<210> 27

<211> 498

<212> DNA

<213> Streptococcus pneumoniae

55

<400> 27

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<211> 732

10 <212> DNA

<213> Streptococcus pneumoniae

<400> 31

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50 <211> 1230

<212> DNA

<213> Streptococcus pneumoniae

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<210> 36

<211> 774

10 <212> DNA

<213> Streptococcus pneumoniae

<400> 36

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 25 aaaggtgata aatttttgcc agcagtagaa agctctaagg ctttcgttta tcgtgctatt 720
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<211> 1239

30 <212> DNA

<213> Streptococcus pneumoniae

<400> 37

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<210> 38

<211> 483

<212> DNA

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<400> 38

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15 <210> 39

<211> 570

<212> DNA

<213> Streptococcus pneumoniae

20 <400> 39

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<210> 40

<211> 852

<212> DNA

35 <213> Streptococcus pneumoniae

<400> 40

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<210> 41

55 <211> 1224

<212> DNA

<213> Streptococcus pneumoniae

<400> 41

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25 <210> 42

<211> 609

<212> DNA

<213> Streptococcus pneumoniae

30 <400> 42

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<210> 43

<211> 1260

45 <212> DNA

<213> Streptococcus pneumoniae

<400> 43

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<210> 44

15 <211> 696

<212> DNA

<213> Streptococcus pneumoniae

<400> 44

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<210> 45

<211> 1125

35 <212> DNA

<213> Streptococcus pneumoniae

<400> 45

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<211> 333

<212> DNA

5 <213> Streptococcus pneumoniae

<400> 46

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15 <210> 47

<211> 672

<212> DNA

<213> Streptococcus pneumoniae

20 <400> 47

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35 <210> 48

<211> 588

<212> DNA

<213> Streptococcus pneumoniae

<400> 48

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50

<210> 49

<211> 294

<212> DNA

<213> Streptococcus pneumoniae

55

<400> 49

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<210> 50

<211> 312

<212> DNA

<213> Streptococcus pneumoniae

<400> 50

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<210> 51

<211> 312

<212> DNA

<213> Streptococcus pneumoniae

<400> 51

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<210> 52

<211> 528

<212> DNA

<213> Streptococcus pneumoniae

<400> 52

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<210> 53

<211> 1368

<212> DNA

<213> Streptococcus pneumoniae

<400> 53

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 <211> 1809

<212> DNA

213> Streptococcus pneumoniae

<400> 56

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<210> 57

<211> 723

<212> DNA

40 <213> Streptococcus pneumoniae

<400> 57

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 55 tga 723

<210> 58

<211> 2223

<212> DNA

<213> Streptococcus pneumoniae

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45 <210> 59

<211> 1479

<212> DNA

<213> Streptococcus pneumoniae

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20 <210> 60
 <211> 1947
 <212> DNA
 <213> Streptococcus pneumoniae

25 <400> 60
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1947

<210> 61

<211> 267

5 <212> DNA

<213> Streptococcus pneumoniae

<400> 61

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 ctcaaaggac aaggagtcca tctataa 267

15 <210> 62

<211> 597

<212> DNA

<213> Streptococcus pneumoniae

20 <400> 62.

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<210> 63

<211> 867

<212> DNA

35 <213> Streptococcus pneumoniae

<400> 63

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<210> 64

55 <211> 420

<212> DNA

<213> Streptococcus pneumoniae

<400> 64

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 gtggctgctg agcgcatgtt gattgaacaa gcagatatca gtcgcaataa gcgcaagaaa 360
 10 gtcattgata agttagcagc tcagctgatt ttacaaaatt atttagatag aaaattttta 420

<210> 65

<211> 1197

<212> DNA

<213> Streptococcus pneumoniae

<400> 65

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<210> 66

<211> 498

<212> DNA

<213> Streptococcus pneumoniae

<400> 66

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 cgttttccta ataccgtatt tgcaggcttt tatttgttgc atggaaagga attggtttta 180
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 tttgaggaaa aatcttaa 498

<210> 67

<211> 630

<212> DNA

<213> Streptococcus pneumoniae

<400> 67

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 5 ctcatgttg cggatcaagt acggcaacag ttgggactgg atcaagttct gctcatgcct 180
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<210> 68

<211> 768

<212> DNA

<213> Streptococcus pneumoniae

<400> 68

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 gatgggtgcag ttgttggttg tattgggttg cttggagacc aagctgtaac agtggttggt 180
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 ctgattaaga gtgtcaaaaa agaactccaa acggagctgg ctgactttc acaaaaaccg 720
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<210> 69

<211> 510

<212> DNA

<213> Streptococcus pneumoniae

<400> 69

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<210> 70

<211> 1590

<212> DNA

<213> Streptococcus pneumoniae

<400> 70

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<210> 71

<211> 468

30 <212> DNA

<213> Streptococcus pneumoniae

<400> 71

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 cccacaaaac aaggatttct tcctatcgaa aatcgtaaac gggggctaga aaaggctttg 180
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 40 catagtcgac ctgaacatct ctatatcagt tcatcaggcg ttagagagct tttgaagttt 420
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<210> 72

<211> 432

45 <212> DNA

<213> Streptococcus pneumoniae

<400> 72

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 55 gtcaagtcag gatctgattt ttatctagta gattttgaaa caggagcatt ggtcaacaag 420
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<210> 73

<211> 732

<212> DNA

<213> Streptococcus pneumoniae

5

<400> 73

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caaataaata gttcacatgt cctcaaatcc aaactttttg gagaacctta taaattcatg 540
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cataatgtgg acggcagacc ccccatatg gcagaagcat atgaccttgt ttcccaaaa 660
tacggagaag cgaaggctca ggaacttttt atagacaatc ctcgaaaaat tgtaatggat 720
caactaattt ag 732

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20

<210> 74

<211> 927

<212> DNA

<213> Streptococcus pneumoniae

25

<400> 74

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45

<210> 75

<211> 234

<212> DNA

<213> Streptococcus pneumoniae

<400> 75

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tttgaacgca gtaaagctcg cggttttgaa gctgtaatgc agcgtttgac agggatttta 180
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55

<210> 76

<211> 1110

<212> DNA

<213> Streptococcus pneumoniae

<400> 76

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<210> 77

25 <211> 1356

<212> DNA

<213> Streptococcus pneumoniae

<400> 77

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<210> 78

55 <211> 1989

<212> DNA

<213> Streptococcus pneumoniae

<400> 78

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	gtgattgggtg	tactggatac	gactatgatg	ttgattgtga	ccttgtctat	ctgcgctatc	1920
35	ttcctcatcg	cctatgtgct	gattttcatg	attacttcaa	gaagttatcg	caagattgtg	1980
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<210> 79

<211> 891

40 <212> DNA

<213> Streptococcus pneumoniae

<400> 79

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	atggcgcaat	ttttagctaa	gagcctcttt	tgtacggata	aagttggcgt	cttaccatgt	180
	gagaaatgcc	gaagttgcaa	gctgattgaa	caggaagagt	ttccagatgt	caccttgatt	240
	aagccagtc	atcaggtcat	caagacagaa	cgcattcggg	aattgggtgg	acagttttct	300
	caagcaggg	ttgaaagcca	gcaacaggtc	tttattatcg	agcaagcgg	taaaatgcat	360
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	ttcttcttga	ctagcgatga	ggaaaagatg	ttaccgacaa	tccgaagtcg	gactcagatc	480
	ttccacttta	aaaagcaaga	agaaaaactt	atcttactct	tagaacaat	gggacttggt	540
	aagaaaaaag	cgactctttt	agctaagttt	agtcaatcgc	gagctgaagc	agaaaagttg	600
	gctaatacagg	caagtttttg	gaccttggtc	gatgaaagtg	aacgcctgct	gacttgggta	660
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	aaggaaaaac	aggatcaggt	tttacggatt	cttgaagttc	tctgtgggca	ggacctcttg	780
	caggtaagag	taagagtgat	tctacaagat	ttactagaag	ctagaaaaat	gtggcaagct	840

aatgtcagct ttcaaaatgc catggaatat ctggtcttga aagaaatata a 891

<210> 80

<211> 615

5' <212> DNA

<213> Streptococcus pneumoniae

<400> 80

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ccgaccctag cggatggcga aattctcttc gttgtaaaac accttcctat tgaccgtttt 180
gatatcgtgg tggcccatga ggaagatggc aataaggaca tctgtcaagcg cgtgattgga 240
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gacgagcctt atctagcaga ctatatcaaa cgcttcaagg atgacaaact ccaaagcact 360
15 tactcaggca agggctttga aggaaataaa ggaactttct ttagaagtat cgctcaaaaa 420
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ggagaatacc ttctcctcgg agatgaccgc ttggtttcga gcgacagccg ccacgtaggt 540
accttcaaag caaaagatat cacaggggaa gctaaattcc gcttctggcc aatcacccgt 600
20 atcggaacat tttaa 615

<210> 81

<211> 987

<212> DNA

<213> Streptococcus pneumoniae

<400> 81

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30 ggtctatttg gtaaaaaacc agcccaagtg gatattgaag cgattagtga aacgactgtt 180
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35 caaactgaaa atcaagactt gaaagagatg ggcttgaagg tcgagcaaag ttatgatatt 540
gccaggtgg ctacggatgt gactgcctat gttcaagcga ttgtggatga catggatgtt 600
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gaaccagggtc gtattatcgg ctaccatggt aaagtcttga aggccttgca actggttggt 720
caaaattatc tttacaaccg ctattccaaa accttctacg ttacaatcaa tgtcaatgat 780
40 tatgtcgaac accgtgcaga agtcttgagc acctatgcgc aaaaattggc gaatcgtgtt 840
ttggaagaag gtcgcagtca taaaacagat ccaatgtcaa atagcgaacg caagattatc 900
catcgtatta tttcacgtat ggatggcgtg actagttact ctgaagggtga tgagccaaat 960
cgctatgttg ttgtagatac agaataa 987

<210> 82

<211> 1383

<212> DNA

<213> Streptococcus pneumoniae

<400> 82

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cataaaaatg tggccactat cttgactgct gaaacggata atccttttgg ctatggacga 420

attgttcgta atgacaatgc tgaggttctt cggtcattgt tgagcagaag gatgctacag 480
 attttgaaaa gcaaatcaag gaaatcaaca ctggtaacat acgtctttga caacgagcgt 540
 ttgtttgagg ctttgaaaaa tatcaatacc aataacgctc aaggcgaata ctatattaca 600
 5' gacgtcattg gtatttttccg tgaaactggg gaaaaagttg gcgcttatac tttgaaagat 660
 tttgatgaaa gtcttggggg aaatgaccgt gtggcgcttg cgacagctga gtcagttatg 720
 cgtcgtcgca tcaatcataa acacatgggc aacgggtgta gctttgtcaa tccagaagca 780
 acttatatcg atattgatgt tgagattgct ccggaagttc aaatcgaagc caatggtatc 840
 ttgaaagggc aaacgaaaat tgggtgctgag actgttttga caaacgggtac ttatgtagtg 900
 gacagcacta tcggagcagg agcgggtcatt accaattcta tgattgagga aagtagtggt 960
 10' gcagacgggtg tgacagtcgg tccttatgct cacattcgtc caaattcaag tctgggtgcc 1020
 caagttcata ttggtaactt tgttgaggtg aaaggatctt caatcgggtg gaataccaag 1080
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 gtctttgttg gttcaaattc aaccattatt gcaccagtag aacttgggtg caattccctc 1260
 15' gttgggtgctg gttcaactat tactaaagac gtgccagcag atgctattgc tattgggtgc 1320
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 tag 1383

20' <210> 83
 <211> 936
 <212> DNA
 <213> Streptococcus pneumoniae

25' <400> 83
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 ggaactccaa atgaagaaac agcctttgtc ttgaactatt ttgggtgtga agcaccaggt 180
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 caccaacag ataaaatcat tgctcctgaa ttggctgaat tggctgggtg aaacttggaa 540
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 aatttcaaac ttgaaaacaa tcatgccttc cttgctgggt ccgtttcacg taagaaacaa 900
 40' gtggtacctc aattaactga aagctttaat acgtaa 936

45' <210> 84
 <211> 678
 <212> DNA
 <213> Streptococcus pneumoniae

50' <400> 84
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 agcgctattg caggtgaggt ggtggaaggt ccctatcagt ctgcgggtta aaatggtgag 180
 gctcaeggcc taaaggagaa aatccaagtc cgtttagcca atggcttggc agcttttgaa 240
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 aatcgtgaag acgacttgcg tatctggcta caggatcatg gattccagat tgtagcagaa 420
 55' agcatcttag aagaagctgg aaagttttat gagatttttg tgggtggaagc aggacaaatg 480
 aagctatcag ccagtgatgt tcgctttggg cccttcttgt ccaaagaagt cagtcagta 540
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gaaaaaaatc tggaagaacg tcaagttcta gtagataaga ttcaagctat caaggagggtg 660
ctccatgtta gcaagtga 678

5 <210> 85
<211> 486
<212> DNA
<213> Streptococcus pneumoniae

10 <400> 85
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ttttcttata aaaatgggac ggatgagttg cagtttagca agaatgaagc gagacctgtg 120
cctgaagttg caactcaagt cgctccagca cccgttctag caacaccgag tccagtagct 180
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gtggctagtg agggaaatct tgtagagagt ccacttggtg gagtggttta cttggctgct 300
15 ggaccagata aacctgcctt cgttacagtt ggtgatagt tcaaaaaagg tcaaacattg 360
gtaattatcg aagccatgaa agtcatgaat gaaatcccag ctccataagga tgggtgtggt 420
acggaaattc tcgtctctaa cgaagaaatg gttgagtttg gtaaaggatt ggtacgtatc 480
aatga 486

20 <210> 86
<211> 1236
<212> DNA
<213> Streptococcus pneumoniae

25 <400> 86
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ccagaagaat tttggaatag tttagcaact gggaaaatcg gcattgggtg cattacaaaa 120
tttgatcata gtgactttga tgtgcataat gcggcagaaa tccaagattt tccgttcgat 180
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30 gcagcccaag aggctgtaaa tcatgccaat cttgatgtag aggctcttaa tagggatcgt 300
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cgccttcacg aaaaaggacc caaacgtgtc aaaccaatga ctcttccaaa agctttacca 420
aatatggctt ctgggaatgt agccatgcgt tttggtgcaa acggtgtttg taaatctatc 480
aatactgcct gctcttcacg aaatgatgcg attggggatg ccttccgctc cattaagttt 540
35 ggtttccaag atgtgatgtt ggtgggagga acagaagctt ctatcacacc ttttgccatc 600
gctggtttcc aagccttaac agctctctct actacagagg atccaactcg tgcttcgatc 660
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45 ggcttggaga aagaaattcc atacgctatt tcaaatactt ttggttttgg aggccacaat 1200
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50 <210> 87
<211> 1080
<212> DNA
<213> Streptococcus pneumoniae

55 <400> 87
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gcttccaatc gtgacaccgt aatagcctac cgtgagtata aacaagtcct tcaaaatata 180
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5 aagcaagaac tcaaagatgc caaggctgaa aaagaagaat atgaagaaaa actgaaaatt 300
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 10 tttaaagaag tggttgctat ggtttcaggt cagtctgtat actctaagct taagtatgaa 540
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<210> 88

<211> 1680

<212> DNA

<213> Streptococcus pneumoniae

20

<400> 88

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 25 attaaattcc cagaagatga cttgcttggg atcgactatg tcattcctga ctactcttac 180
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<210> 89

<211> 1362

<212> DNA

<213> Streptococcus pneumoniae

55

<400> 89

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	cgggactttt	ttaagtatgc	ccatcgtttg	attttccaag	ccatggtcga	tttatccgat	180
	cgtggtgatg	ccatagatgc	aacaacgggt	cgtactatcc	ttgataatca	aggtgattta	240
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	aagttgacag	agtctgtcaa	ccaagcttac	gaagcgtcac	aaccagctga	tgaaattatt	420
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	gagaaaaacc	gtagtggagc	tcgtggaaca	gtggaattga	ttgtccaaaa	agaatacaat	1320
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<210> 90

25 <211> 693

<212> DNA

<213> Streptococcus pneumoniae

<400> 90

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<211> 978

25 <212> DNA

<213> Streptococcus pneumoniae

<400> 94

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<211> 750

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50 <213> Streptococcus pneumoniae

<400> 95

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<211> 921

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15 <213> Streptococcus pneumoniae

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<211> 741

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<213> Streptococcus pneumoniae

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<213> Streptococcus pneumoniae

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20 <211> 1623

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<213> Streptococcus pneumoniae

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55 <211> 1446

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30 <211> 1980

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 ttggaacgta agaaggtctt gaaggtttac gacccaagtc aacacgacta tgagactgat 840
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<211> 1275

<212> DNA

<213> Streptococcus pneumoniae

25

<400> 109

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 30 tcgctggttc cggaggtagt tgtcaacggg caggaataca ccgttcccta tgtgacagaa 240
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 aatcaagcct atccttctat cgttaaacgt gggggtgggg cgcgtgatct gcatgtcgag 480
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50

<210> 110

<211> 789

<212> DNA

<213> Streptococcus pneumoniae

55

<400> 110

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5 cgtgcgaatc atgataaaaa tttgcgtatt aagagtttag aagagcgttt gtcttacttt 180
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 10 aaagaattgt ctgaatttga agctcagatt aaacaggaag tggaagctcc aactcctgta 720
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<210> 111

15 <211> 1728

<212> DNA

<213> Streptococcus pneumoniae

<400> 111

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 35 atttttactc gagaaattgc tgctcagaaa gtagtggaat atctacttgc aactcttcca 960
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 45 caatatgcaa ctttgacaga gcaactcttg caatattcta accgctatcg ctcatattgat 1560
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 cacgcttcat ttgataagat ttctcaagca ttggaagtgg cagagcctgg tgtaaccaat 1680
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<211> 2403

<212> DNA

<213> Streptococcus pneumoniae

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5 ggtctctcaa aaattgtcgt cggtagaggtc ttgtcttgcg aagatgtgcc agagactcac 180
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<211> 543

<212> DNA

<213> Streptococcus pneumoniae

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<400> 113

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 55 gcagactata cctgctttac tatcccaaat gagttttag taggttatgg tttagactac 480
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 tag 543

<210> 114
 <211> 235
 <212> PRT
 <213> Streptococcus pneumoniae

5

<400> 114
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10 Ile Ser Asn Leu Pro Lys Gln Phe Leu Glu Leu Gly Asp Arg Pro Ile
 20 25 30

Leu Ile His Thr Ile Glu Lys Phe Val Leu Glu Pro Ser Ile Glu Lys
 35 40 45

15

Ile Val Val Gly Val His Gly Asp Trp Val Leu His Ala Glu Asp Leu
 50 55 60

20 Val Asp Lys Tyr Leu Pro Leu His Lys Glu Arg Ile Ile Ile Thr Lys
 65 70 75 80

Gly Gly Ala Asp Arg Asn Thr Ser Ile Glu Asn Ile Ile Glu Ala Ile
 85 90 95

25 Asp Ala Tyr Arg Pro Leu Thr Pro Glu Asp Ile Val Val Thr His Asp
 100 105 110

Ser Val Arg Pro Phe Ile Thr Leu Arg Met Ile Gln Asp Ser Ile Lys
 115 120 125

30

Leu Ala Gln Asn His Asp Ala Val Asp Thr Val Val Glu Ala Val Asp
 130 135 140

35 Thr Ile Val Glu Ser Thr Asn Gly Gln Phe Ile Thr Gly Ile Pro Asn
 145 150 155 160

Arg Ala His Leu Tyr Gln Gly Gln Thr Pro Gln Thr Phe Arg Cys Lys
 165 170 175

40 Asp Phe Met Asp Leu Tyr Gly Ser Leu Ser Asp Glu Glu Lys Glu Ile
 180 185 190

Leu Thr Asp Ala Cys Lys Ile Phe Val Ile Lys Gly Lys Asp Val Ala
 195 200 205

45

Leu Ala Lys Gly Glu Tyr Ser Asn Leu Lys Ile Thr Thr Val Thr Asp
 210 215 220

50 Leu Lys Ile Ala Lys Ser Met Ile Glu Lys Asp
 225 230 235

<210> 115
 <211> 185
 <212> PRT
 <213> Streptococcus pneumoniae

55

<400> 115

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5 His Gln Ser Leu Ala Arg Glu Phe Gly Gly Ile Arg Ala Gly Arg Ala
 20 25 30

Asn Ala Ser Leu Leu Asp Arg Val His Val Glu Tyr Tyr Gly Val Glu
 35 40 45

10 Thr Pro Leu Asn Gln Ile Ala Ser Ile Thr Ile Pro Glu Ala Arg Val
 50 55 60

15 Leu Leu Val Thr Pro Phe Asp Lys Ser Ser Leu Lys Asp Ile Glu Arg
 65 70 75 80

Ala Leu Asn Ala Ser Asp Leu Gly Ile Thr Pro Ala Asn Asp Gly Ser
 85 90 95

20 Val Ile Arg Leu Val Ile Pro Ala Leu Thr Glu Glu Thr Arg Arg Asp
 100 105 110

Leu Ala Lys Glu Val Lys Lys Val Gly Glu Asn Ala Lys Val Ala Val
 115 120 125

25 Arg Asn Ile Arg Arg Asp Ala Met Asp Glu Ala Lys Lys Gln Glu Lys
 130 135 140

30 Ala Gln Glu Ile Thr Glu Asp Glu Leu Lys Thr Leu Glu Lys Asp Ile
 145 150 155 160

Gln Lys Val Thr Asp Asp Ala Val Lys His Ile Asp Asp Met Thr Ala
 165 170 175

35 Asn Lys Glu Lys Glu Leu Leu Glu Val
 180 185

<210> 116

<211> 450

<212> PRT

<213> Streptococcus pneumoniae

<400> 116

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 20 25 30

50 Val Leu Ser Gln His Glu Thr Glu Ala Pro Lys Val Phe Val Gly Arg
 35 40 45

55 Asp Thr Arg Ile Ser Gly Glu Met Leu Glu Ser Ala Leu Val Ala Gly
 50 55 60

Leu Leu Ser Val Gly Ile His Val Tyr Lys Leu Gly Val Leu Ala Thr

	65		70		75		80
	Pro	Ala	Val	Ala	Tyr	Leu	Val
				85			
5	Met	Ile	Ser	Ala	Ser	His	Asn
			100				
	Phe	Gly	Gly	Asp	Gly	Phe	Lys
10			115				
	Glu	Ala	Leu	Leu	Asp	Ala	Glu
			130				
15	Glu	Gly	Leu	Gly	Ile	Leu	Val
			145				
	Glu	Gly	Tyr	Arg	Val	Ser	Thr
20							
	Ala	Leu	Asp	Thr	Ala	Asn	Gly
25	Phe	Ala	Asp	Leu	Gly	Ala	Gln
			195				
	Gly	Leu	Asn	Ile	Asn	Leu	Asn
			210				
30	Gln	Glu	Val	Val	Lys	Glu	Ser
	Gly	Asp	Ser	Asp	Arg	Leu	Ile
35							
	Asp	Gly	Asp	Lys	Ile	Met	Tyr
40	Gly	Gln	Leu	Ala	Gln	Asn	Thr
			275				
	Gly	Phe	His	Lys	Ala	Leu	Asn
45	Ala	Val	Gly	Asp	Arg	Tyr	Val
	Asn	Leu	Gly	Gly	Glu	Gln	Ser
50							
	Thr	Thr	Gly	Asp	Gly	Gln	Leu
55	Lys	Glu	Thr	Gly	Lys	Ser	Leu
	Tyr	Pro	Gln	Lys	Leu	Val	Asn

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	Glu Glu Met Ala Gly 405	Asn Gly Arg Ile Leu 410	Ile Ile Glu Lys Met Glu 400
10	Glu Pro Leu 420	Leu Arg Val Met Ala Glu 425	Ala Pro Thr Thr Glu Glu Val 430
	Asp Tyr Tyr 435	Val Asp Thr Ile Thr 440	Val Arg Ala Glu Ile Gly 445
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	Asn Gly Arg 35	Glu Ala Leu Glu Gln Phe Glu Ala Glu Gln Pro Asp Ile 40 45	
35	Ile Ile Leu 50	Asp Leu Met Leu Pro Glu Ile Asp Gly Leu Glu Val Ala 55 60	
	Lys Thr Ile 65	Arg Lys Thr Ser Ser Val Pro Ile Leu Met Leu Ser Ala 70 75 80	
40	Lys Asp Ser Glu Phe 85	Asp Lys Val Ile Gly Leu Glu Leu Gly Ala Asp 90 95	
45	Asp Tyr Val 100	Thr Lys Pro Phe Ser Asn Arg Glu Leu Gln Ala Arg Val 105 110	
	Lys Ala Leu 115	Leu Arg Arg Ser Gln Pro Met Pro Val Asp Gly Gln Glu 120 125	
50	Ala Asp Ser Lys Pro Gln Pro 130 135	Ile Gln Ile Gly Asp Leu Glu Ile Val 140	
	Pro Asp Ala Tyr Val 145	Ala Lys Lys Tyr Gly Glu Glu Leu Asp Leu Thr 150 155 160	
55	His Arg Glu Phe 165	Glu Leu Leu Tyr His Leu Ala Ser His Thr Gly Gln 170 175	

Val Ile Thr Arg Glu His Leu Leu Glu Thr Val Trp Gly Tyr Asp Tyr
 180 185 190
 5 Phe Gly Asp Val Arg Thr Val Asp Val Thr Val Arg Arg Leu Arg Glu
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 Lys Ile Glu Asp Thr Pro Ser Arg Pro Glu Tyr Ile Leu Thr Arg Arg
 210 215 220
 10 Gly Val Gly Tyr Tyr Met Arg Asn Asn Ala
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 Asp Lys Ala Gly Leu Gly Phe Thr Pro Gln Ser Ala Leu Glu Lys Gly
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 35 40 45
 Tyr Asn Glu Ile Thr Asp Val Gln Leu Thr Asn Asp Asp Phe Leu Lys
 50 55 60
 30 Leu Leu His Glu Val Gly Asp Ser Asp Ala Leu Val Val Asn Val Ile
 65 70 75 80
 35 Asp Ile Phe Asp Phe Asn Gly Ser Val Ile Pro Gly Leu Pro Arg Phe
 85 90 95
 Val Ser Gly Asn Asp Val Leu Leu Val Gly Asn Lys Lys Asp Ile Leu
 100 105 110
 40 Pro Lys Ser Val Lys Ser Gly Lys Ile Ser Gln Trp Leu Met Lys Arg
 115 120 125
 Ala His Glu Glu Gly Leu Arg Pro Val Asp Val Val Leu Thr Ser Ala
 130 135 140
 45 Gln Asn Lys His Ala Ile Lys Glu Val Ile Asp Lys Ile Glu His Tyr
 145 150 155 160
 50 Arg Lys Gly Arg Asp Val Tyr Val Val Gly Val Thr Asn Val Gly Lys
 165 170 175
 Ser Thr Leu Ile Asn Ala Ile Ile Gln Glu Ile Thr Gly Asp Gln Asn
 180 185 190
 55 Val Ile Thr Thr Ser Arg Phe Pro Gly Thr Thr Leu Asp Lys Ile Glu
 195 200 205

Ile Pro Leu Asp Asp Gly Ser Tyr Ile Tyr Asp Thr Pro Gly Ile Ile
 210 215 220
 5 His Arg His Gln Met Ala His Tyr Leu Thr Ala Lys Asn Leu Lys Tyr
 225 230 235 240
 Val Ser Pro Lys Lys Glu Ile Lys Pro Lys Thr Tyr Gln Leu Asn Pro
 245 250 255
 10 Glu Gln Thr Leu Phe Leu Gly Gly Leu Gly Arg Phe Asp Phe Ile Ala
 260 265 270
 Gly Glu Lys Gln Gly Phe Thr Ala Phe Phe Asp Asn Glu Leu Lys Leu
 275 280 285
 15 His Arg Ser Lys Leu Glu Gly Ala Ser Ala Phe Tyr Asp Lys His Leu
 290 295 300
 20 Gly Thr Leu Leu Thr Pro Pro Asn Ser Lys Glu Lys Glu Asp Phe Pro
 305 310 315 320
 Arg Leu Val Gln His Val Phe Thr Ile Lys Asp Lys Thr Asp Leu Val
 325 330 335
 25 Ile Ser Gly Leu Gly Trp Ile Arg Val Thr Gly Thr Ala Lys Val Ala
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 Val Trp Ala Pro Glu Gly Val Ala Val Val Thr Arg Lys Ala Ile Ile
 355 360 365
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 <211> 486
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 <213> Streptococcus pneumoniae
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 35 40 45
 50 Val Phe Ala Gly Leu Glu Arg Ile Val Asn Tyr Leu Glu Asp Leu Arg
 50 55 60
 Phe Ser Asp Ser Asp Ile Ala Tyr Leu Glu Ser Leu Gly Tyr His Gly
 65 70 75 80
 55 Ala Phe Leu Asp Tyr Leu Arg Asn Phe Lys Leu Glu Leu Thr Val Arg

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5	Ser Ala Gln Glu Gly Asp Leu Val Phe Ala Asn Glu Pro Ile Val Gln 100 105 110		
	Val Glu Gly Pro Leu Ala Gln Cys Gln Leu Val Glu Thr Ala Leu Leu 115 120 125		
10	Asn Ile Val Asn Tyr Gln Thr Leu Val Ala Thr Lys Ala Ala Arg Ile 130 135 140		
	Arg Ser Val Ile Glu Asp Glu Pro Leu Met Glu Phe Gly Thr Arg Arg 145 150 155 160		
15	Ala Gln Glu Thr Asp Ala Ala Ile Trp Gly Thr Arg Ala Ala Val Ile 165 170 175		
	Gly Gly Ala Asn Gly Thr Ser Asn Val Arg Ala Gly Lys Leu Phe Asp 180 185 190		
20	Ile Pro Val Leu Gly Thr His Ala His Ala Leu Val Gln Val Tyr Gly 195 200 205		
25	Asn Asp Tyr Glu Ala Phe Lys Ala Tyr Ala Ala Thr His Lys Asn Cys 210 215 220		
	Val Phe Leu Val Asp Thr Tyr Asp Thr Leu Arg Ile Gly Val Pro Ala 225 230 235 240		
30	Ala Ile Gln Val Ala Arg Glu Leu Gly Asp Gln Ile Asn Phe Met Gly 245 250 255		
	Val Arg Ile Asp Ser Gly Asp Ile Ala Tyr Ile Ser Lys Lys Val Arg 260 265 270		
35	Gln Gln Leu Asp Glu Ala Gly Phe Thr Glu Ala Lys Ile Tyr Ala Ser 275 280 285		
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45	Gln Pro Ala Leu Gly Ala Val Tyr Lys Ile Val Ala Ile Glu Asp Glu 325 330 335		
	Thr Gly Gln Met Arg Asn Thr Ile Lys Leu Ser Asn Asn Ala Glu Lys 340 345 350		
50	Val Ser Thr Pro Gly Lys Lys Gln Val Trp Arg Ile Thr Ser Arg Glu 355 360 365		
55	Lys Gly Lys Ser Glu Gly Asp Tyr Ile Thr Tyr Asp Gly Val Asp Ile 370 375 380		
	Ser Asp Met Thr Glu Ile Lys Met Phe His Pro Thr Tyr Thr Tyr Ile		

	385		390		395		400									
	Lys	Lys	Thr	Val	Arg	Asn	Phe	Asp	Ala	Val	Pro	Leu	Leu	Val	Asp	Ile
					405					410					415	
5	Phe	Lys	Glu	Gly	Ile	Leu	Val	Tyr	Asn	Leu	Pro	Ser	Leu	Thr	Asp	Ile
				420					425					430		
10	Gln	Asp	Tyr	Ala	Arg	Lys	Glu	Phe	Asp	Lys	Leu	Trp	Asp	Glu	Tyr	Lys
			435					440					445			
	Arg	Val	Leu	Asn	Pro	Gln	His	Tyr	Pro	Val	Asp	Leu	Ala	Arg	Asp	Val
		450					455					460				
15	Trp	Gln	Asp	Lys	Met	Asp	Leu	Ile	Asp	Lys	Met	Arg	Lys	Glu	Ala	Leu
	465					470					475					480
	Gly	Glu	Gly	Glu	Glu	Glu										
					485											
20																
	<210>	120														
	<211>	283														
	<212>	PRT														
25	<213>	Streptococcus pneumoniae														
	<400>	120														
	Met	Ala	Thr	Ile	Gln	Trp	Phe	Pro	Gly	His	Met	Ser	Lys	Ala	Arg	Arg
	1				5					10					15	
30	Gln	Val	Gln	Glu	Asn	Leu	Lys	Phe	Val	Asp	Phe	Val	Thr	Ile	Leu	Val
				20					25					30		
35	Asp	Ala	Arg	Leu	Pro	Leu	Ser	Ser	Gln	Asn	Pro	Met	Leu	Thr	Lys	Ile
			35					40					45			
	Val	Gly	Asp	Lys	Pro	Lys	Leu	Leu	Ile	Leu	Asn	Lys	Ala	Asp	Leu	Ala
		50					55					60				
40	Asp	Pro	Ala	Met	Thr	Lys	Glu	Trp	Arg	Gln	Tyr	Phe	Glu	Ser	Gln	Gly
	65					70					75					80
	Ile	Gln	Thr	Leu	Ala	Ile	Asn	Ser	Lys	Glu	Gln	Val	Thr	Val	Lys	Val
					85					90					95	
45	Val	Thr	Asp	Ala	Ala	Lys	Lys	Leu	Met	Ala	Asp	Lys	Ile	Ala	Arg	Gln
				100					105					110		
50	Lys	Glu	Arg	Gly	Ile	Gln	Ile	Glu	Thr	Leu	Arg	Thr	Met	Ile	Ile	Gly
			115					120					125			
	Ile	Pro	Asn	Ala	Gly	Lys	Ser	Thr	Leu	Met	Asn	Arg	Leu	Ala	Gly	Lys
		130					135					140				
55	Lys	Ile	Ala	Val	Val	Gly	Asn	Lys	Pro	Gly	Val	Thr	Lys	Gly	Gln	Gln
	145					150					155					160

Trp Leu Lys Thr Asn Lys Asp Leu Glu Ile Leu Asp Thr Pro Gly Ile
 165 170 175

5 Leu Trp Pro Lys Phe Glu Asp Glu Thr Val Ala Leu Lys Leu Ala Leu
 180 185 190

Thr Gly Ala Ile Lys Asp Gln Leu Leu Pro Met Asp Glu Val Thr Ile
 195 200 205

10 Phe Gly Ile Asn Tyr Phe Lys Glu His Tyr Pro Glu Lys Leu Ala Glu
 210 215 220

Arg Phe Lys Gln Met Lys Ile Glu Glu Glu Pro Ser Val Ile Ile Met
 225 230 235 240

15 Asp Met Thr Arg Ala Leu Gly Phe Arg Asp Asp Tyr Asp Arg Phe Tyr
 245 250 255

20 Ser Leu Phe Val Lys Glu Val Arg Asp Gly Lys Leu Gly Asn Tyr Thr
 260 265 270

Leu Asp Thr Leu Glu Asp Leu Asp Gly Asn Asp
 275 280

25
 <210> 121
 <211> 156
 <212> PRT
 <213> Streptococcus pneumoniae

30
 <400> 121
 Met Ile Asn Asn Val Val Leu Val Gly Arg Met Thr Arg Asp Ala Glu
 1 5 10 15

35 Leu Arg Tyr Thr Pro Ser Asn Val Ala Val Ala Thr Phe Thr Leu Ala
 20 25 30

Val Asn Arg Thr Phe Lys Ser Gln Asn Gly Glu Arg Glu Ala Asp Phe
 35 40 45

40 Ile Asn Val Val Met Trp Arg Gln Gln Ala Glu Asn Leu Ala Asn Trp
 50 55 60

45 Ala Lys Lys Gly Ser Leu Ile Gly Val Thr Gly Arg Ile Gln Thr Arg
 65 70 75 80

Ser Tyr Asp Asn Gln Gln Gly Gln Arg Val Tyr Val Thr Glu Val Val
 85 90 95

50 Ala Glu Asn Phe Gln Met Leu Glu Ser Arg Ser Val Arg Glu Gly His
 100 105 110

Thr Gly Gly Ala Tyr Ser Ala Pro Thr Ala Asn Tyr Ser Ala Pro Thr
 115 120 125

55 Asn Ser Val Pro Asp Phe Ser Arg Asn Glu Asn Pro Phe Gly Ala Thr
 130 135 140

Asn Pro Leu Asp Ile Ser Asp Asp Asp Leu Pro Phe
 145 150 155

5
 <210> 122
 <211> 324
 <212> PRT
 <213> Streptococcus pneumoniae

10
 <400> 122
 Met Lys Thr Arg Ile Thr Glu Leu Leu Lys Ile Asp Tyr Pro Ile Phe
 1 5 10 15

15
 Gln Gly Gly Met Ala Trp Val Ala Asp Gly Asp Leu Ala Gly Ala Val
 20 25 30

20
 Ser Lys Ala Gly Gly Leu Gly Ile Ile Gly Gly Gly Asn Ala Pro Lys
 35 40 45

25
 Glu Val Val Lys Ala Asn Ile Asp Lys Ile Lys Ser Leu Thr Asp Lys
 50 55 60

30
 Pro Phe Gly Val Asn Ile Met Leu Leu Ser Pro Phe Val Glu Asp Ile
 65 70 75 80

35
 Val Asp Leu Val Ile Glu Glu Gly Val Lys Val Val Thr Thr Gly Ala
 85 90 95

40
 Gly Asn Pro Ser Lys Tyr Met Glu Arg Phe His Glu Ala Gly Ile Ile
 100 105 110

45
 Val Ile Pro Val Val Pro Ser Val Ala Leu Ala Lys Arg Met Glu Lys
 115 120 125

50
 Ile Gly Ala Asp Ala Val Ile Ala Glu Gly Met Glu Ala Gly Gly His
 130 135 140

55
 Ile Gly Lys Leu Thr Thr Met Thr Leu Val Arg Gln Val Ala Thr Ala
 145 150 155 160

60
 Ile Ser Ile Pro Val Ile Ala Ala Gly Gly Ile Ala Asp Gly Glu Gly
 165 170 175

65
 Ala Ala Ala Gly Phe Met Leu Gly Ala Glu Ala Val Gln Val Gly Thr
 180 185 190

70
 Arg Phe Val Val Ala Lys Glu Ser Asn Ala His Pro Asn Tyr Lys Glu
 195 200 205

75
 Lys Ile Leu Lys Ala Arg Asp Ile Asp Thr Thr Ile Ser Ala Gln His
 210 215 220

80
 Phe Gly His Ala Val Arg Ala Ile Lys Asn Gln Leu Thr Arg Asp Phe
 225 230 235 240

85
 Glu Leu Ala Glu Lys Asp Ala Phe Lys Gln Glu Asp Pro Asp Leu Glu

	245	250	255
	Ile Phe Glu Gln Met Gly Ala Gly Ala Leu Ala Lys Ala Val Val His		
5	260	265	270
	Gly Asp Val Glu Gly Gly Ser Val Met Ala Gly Gln Ile Ala Gly Leu		
	275	280	285
10	Val Ser Lys Glu Glu Thr Ala Glu Glu Ile Leu Lys Asp Leu Tyr Tyr		
	290	295	300
	Gly Ala Ala Lys Lys Ile Gln Glu Glu Ala Ser Arg Trp Thr Gly Val		
	305	310	315
15	Val Arg Asn Asp		
20	<210> 123		
	<211> 140		
	<212> PRT		
	<213> Streptococcus pneumoniae		
25	<400> 123		
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	1	5	10
	Met Leu Leu Val Asp Arg Val Leu Glu Val Ser Glu Asp Thr Ile Val		
30	20	25	30
	Ala Ile Lys Asn Val Thr Ile Asn Glu Pro Phe Phe Asn Gly His Phe		
	35	40	45
35	Pro Gln Tyr Pro Val Met Pro Gly Val Leu Ile Met Glu Ala Leu Ala		
	50	55	60
	Gln Thr Ala Gly Val Leu Glu Leu Ser Lys Pro Glu Asn Lys Gly Lys		
	65	70	75
40	Leu Val Phe Tyr Ala Gly Met Asp Lys Val Lys Phe Lys Lys Gln Val		
	85	90	95
	Val Pro Gly Asp Gln Leu Val Met Thr Ala Thr Phe Val Lys Arg Arg		
45	100	105	110
	Gly Thr Ile Ala Val Val Glu Ala Lys Ala Glu Val Asp Gly Lys Leu		
	115	120	125
50	Ala Ala Ser Gly Thr Leu Thr Phe Ala Ile Gly Asn		
	130	135	140
55	<210> 124		
	<211> 340		
	<212> PRT		
	<213> Streptococcus pneumoniae		

<400> 124
 Met Ile Asn Gln Ile Tyr Gln Leu Thr Lys Pro Lys Phe Ile Asn Val
 1 5 10 15
 5 Lys Tyr Gln Glu Glu Ala Ile Asp Gln Glu Asn His Ile Leu Ile Arg
 20 25 30
 Pro Asn Tyr Met Ala Val Cys His Ala Asp Gln Arg Tyr Tyr Gln Gly
 35 40 45
 10 Lys Arg Asp Pro Lys Ile Leu Asn Lys Lys Leu Pro Met Ala Met Ile
 50 55 60
 15 His Glu Ser Cys Gly Ile Val Ile Ser Asp Pro Ser Gly Thr Tyr Glu
 65 70 75 80
 Val Gly Gln Lys Val Val Met Ile Pro Asn Gln Ser Pro Met Gln Ser
 85 90 95
 20 Asp Glu Glu Phe Tyr Glu Asn Tyr Met Thr Gly Thr His Phe Leu Ser
 100 105 110
 Ser Gly Phe Asp Gly Phe Met Arg Glu Phe Val Ser Leu Pro Lys Asp
 115 120 125
 25 Arg Val Val Ala Tyr Asp Ala Ile Glu Asp Thr Val Ala Ala Ile Thr
 130 135 140
 30 Glu Phe Val Ser Val Gly Met His Ala Met Asn Arg Leu Leu Thr Leu
 145 150 155 160
 Ala His Ser Lys Arg Glu Arg Ile Pro Val Ile Gly Asp Gly Ser Leu
 165 170 175
 35 Ala Phe Val Val Ala Asn Ile Ile Asn Tyr Thr Leu Pro Glu Ala Glu
 180 185 190
 Ile Val Val Ile Gly Arg His Trp Glu Lys Leu Glu Leu Phe Ser Phe
 195 200 205
 40 Ala Lys Glu Cys Tyr Ile Thr Asp Asn Ile Pro Glu Glu Leu Ala Phe
 210 215 220
 45 Asp His Ala Phe Glu Cys Cys Gly Gly Asp Gly Thr Gly Pro Ala Ile
 225 230 235 240
 Asn Asp Leu Ile Arg Tyr Ile Arg Pro Gln Gly Thr Ile Leu Met Met
 245 250 255
 50 Gly Val Ser Glu Tyr Lys Val Asn Leu Asn Thr Arg Asp Ala Leu Glu
 260 265 270
 Lys Gly Leu Leu Leu Val Gly Ser Ser Arg Ser Gly Arg Ile Asp Phe
 275 280 285
 55 Glu Asn Ala Ile Gln Met Met Lys Val Lys Lys Phe Ala Asn Arg Leu
 290 295 300

Lys Asn Ile Leu Tyr Leu Glu Glu Pro Val Arg Glu Ile Lys Asp Ile
 305 310 315 320
 5 His Arg Val Phe Ala Thr Asp Leu Asn Thr Ala Phe Lys Thr Val Phe
 325 330 335
 Lys Trp Glu Val
 340
 10
 <210> 125
 <211> 447
 <212> PRT
 15 <213> Streptococcus pneumoniae
 <400> 125
 Met Asn Leu Lys Thr Thr Leu Gly Leu Leu Ala Gly Arg Ser Ser His
 1 5 10 15
 20 Phe Val Leu Ser Arg Leu Gly Arg Gly Ser Thr Leu Pro Gly Lys Val
 20 25 30
 25 Ala Leu Gln Phe Asp Lys Asp Ile Leu Gln Asn Leu Ala Lys Asn Tyr
 35 40 45
 Glu Ile Val Val Val Thr Gly Thr Asn Gly Lys Thr Leu Thr Thr Ala
 50 55 60
 30 Leu Thr Val Gly Ile Leu Lys Glu Val Tyr Gly Gln Val Leu Thr Asn
 65 70 75 80
 Pro Ser Gly Ala Asn Met Ile Thr Gly Ile Ala Thr Thr Phe Leu Thr
 85 90 95
 35 Ala Lys Ser Ser Lys Thr Gly Lys Asn Ile Ala Val Leu Glu Ile Asp
 100 105 110
 40 Glu Ala Ser Leu Ser Arg Ile Cys Asp Tyr Ile Gln Pro Ser Leu Phe
 115 120 125
 Val Ile Thr Asn Ile Phe Arg Asp Gln Met Asp Arg Phe Gly Glu Ile
 130 135 140
 45 Tyr Thr Thr Tyr Asn Met Ile Leu Asp Ala Ile Arg Lys Val Pro Thr
 145 150 155 160
 Ala Thr Val Leu Leu Asn Gly Asp Ser Pro Leu Phe Tyr Lys Pro Thr
 165 170 175
 50 Ile Pro Asn Pro Ile Glu Tyr Phe Gly Phe Asp Leu Glu Lys Gly Pro
 180 185 190
 55 Ala Gln Leu Ala His Tyr Asn Thr Glu Gly Ile Leu Cys Pro Asp Cys
 195 200 205
 Gln Gly Ile Leu Lys Tyr Glu His Asn Thr Tyr Ala Asn Leu Gly Ala

	210	215	220
5	Tyr Ile Cys Glu Gly Cys Gly Cys Lys Arg Pro Asp Leu Asp Tyr Arg 225 230 235 240		
	Leu Thr Lys Leu Val Glu Leu Thr Asn Asn Arg Ser Arg Phe Val Ile 245 250 255		
10	Asp Gly Gln Glu Tyr Gly Ile Gln Ile Gly Gly Leu Tyr Asn Ile Tyr 260 265 270		
	Asn Ala Leu Ala Ala Val Ala Ile Ala Arg Phe Leu Gly Ala Asp Ser 275 280 285		
15	Gln Leu Ile Lys Gln Gly Phe Asp Lys Ser Arg Ala Val Phe Gly Arg 290 295 300		
20	Gln Glu Thr Phe His Ile Gly Asp Lys Glu Cys Thr Leu Val Leu Ile 305 310 315 320		
	Lys Asn Pro Val Gly Ala Thr Gln Ala Ile Glu Met Ile Lys Leu Ala 325 330 335		
25	Pro Tyr Pro Phe Ser Leu Ser Val Leu Leu Asn Ala Asn Tyr Ala Asp 340 345 350		
	Gly Ile Asp Thr Ser Trp Ile Trp Asp Ala Asp Phe Glu Gln Ile Thr 355 360 365		
30	Asp Met Asp Ile Pro Glu Ile Asn Ala Gly Gly Val Arg His Ser Glu 370 375 380		
35	Ile Ala Arg Arg Leu Arg Val Thr Gly Tyr Pro Ala Glu Lys Ile Thr 385 390 395 400		
	Glu Thr Ser Asn Leu Glu Gln Val Leu Lys Thr Ile Glu Asn Gln Asp 405 410 415		
40	Cys Lys His Ala Tyr Ile Leu Ala Thr Tyr Thr Ala Met Leu Glu Phe 420 425 430		
	Arg Glu Leu Leu Ala Ser Arg Gln Ile Val Arg Lys Glu Met Asn 435 440 445		
45	<210> 126 <211> 260 <212> PRT <213> Streptococcus pneumoniae		
50	<400> 126 Met Val Tyr Thr Ser Leu Ser Ser Lys Asp Gly Asn Tyr Pro Tyr Gln 1 5 10 15		
55	Leu Asn Ile Ala His Leu Tyr Gly Asn Leu Met Asn Thr Tyr Gly Asp 20 25 30		

Asn Gly Asn Ile Leu Met Leu Lys Tyr Val Ala Glu Lys Leu Gly Ala
 35 40 45
 5 His Val Thr Val Asp Ile Val Ser Leu His Asp Asp Phe Asp Glu Asn
 50 55 60
 His Tyr Asp Ile Ala Phe Phe Gly Gly Gly Gln Asp Phe Glu Gln Ser
 65 70 75 80
 10 Ile Ile Ala Asp Asp Leu Pro Ala Lys Lys Glu Ser Ile Asp Asn Tyr
 85 90 95
 Ile Gln Asn Asp Gly Val Val Leu Ala Ile Cys Gly Gly Phe Gln Leu
 100 105 110
 15 Leu Gly Gln Tyr Tyr Val Glu Ala Ser Gly Lys Arg Ile Glu Gly Leu
 115 120 125
 20 Gly Val Met Gly His Tyr Thr Leu Asn Gln Thr Asn Asn Arg Phe Ile
 130 135 140
 Gly Asp Ile Lys Ile His Asn Glu Asp Phe Asp Glu Thr Tyr Tyr Gly
 145 150 155 160
 25 Phe Glu Asn His Gln Gly Arg Thr Phe Leu Ser Asp Asp Gln Lys Pro
 165 170 175
 Leu Gly Gln Val Val Tyr Gly Asn Gly Asn Asn Glu Glu Lys Val Gly
 180 185 190
 30 Glu Gly Val His Tyr Lys Asn Val Phe Gly Ser Tyr Phe His Gly Pro
 195 200 205
 35 Ile Leu Ser Arg Asn Ala Asn Leu Ala Tyr Arg Leu Val Thr Thr Ala
 210 215 220
 Leu Lys Lys Lys Tyr Gly Gln Asp Ile Gln Leu Pro Ala Tyr Glu Asp
 225 230 235 240
 40 Ile Leu Ser Gln Glu Ile Ala Glu Glu Tyr Ser Asp Val Lys Ser Lys
 245 250 255
 Ala Asp Phe Ser
 260
 45
 <210> 127
 <211> 223
 <212> PRT
 50 <213> Streptococcus pneumoniae
 <400> 127
 Met Asn Val Lys Glu Asn Thr Glu Leu Val Phe Arg Glu Val Ala Glu
 1 5 10 15
 55 Ala Ser Leu Ser Ala Asn Arg Glu Ser Gly Ser Val Ser Val Ile Ala
 20 25 30

Val Thr Lys Tyr Val Asp Val Pro Thr Ala Glu Ala Leu Leu Pro Leu
 35 40 45
 5 Gly Val His His Ile Gly Glu Asn Arg Val Asp Lys Phe Leu Glu Lys
 50 55 60
 Tyr Glu Ala Leu Lys Asp Arg Asp Val Thr Trp His Leu Ile Gly Thr
 65 70 75 80
 10 Leu Gln Arg Arg Lys Val Lys Asp Val Ile Gln Tyr Val Asp Tyr Phe
 85 90 95
 15 His Ala Leu Asp Ser Val Lys Leu Ala Gly Glu Ile Gln Lys Arg Ser
 100 105 110
 Asp Arg Val Ile Lys Cys Phe Leu Gln Val Asn Ile Ser Lys Glu Glu
 115 120 125
 20 Ser Lys His Gly Phe Ser Arg Glu Glu Leu Leu Glu Ile Leu Pro Glu
 130 135 140
 Leu Ala Gly Leu Asp Lys Ile Glu Tyr Val Gly Leu Met Thr Met Ala
 145 150 155 160
 25 Pro Phe Glu Ala Ser Ser Glu Gln Leu Lys Glu Ile Phe Lys Ala Ala
 165 170 175
 30 Gln Asp Leu Gln Arg Glu Ile Gln Glu Lys Gln Ile Pro Asn Ile Pro
 180 185 190
 Met Thr Glu Leu Ser Met Gly Met Ser Arg Asp Tyr Lys Glu Ala Ile
 195 200 205
 35 Gln Phe Gly Ser Thr Phe Val Arg Ile Gly Thr Ser Phe Phe Lys
 210 215 220
 40 <210> 128
 <211> 279
 <212> PRT
 <213> Streptococcus pneumoniae
 45 <400> 128
 Met Gly Ile Ala Leu Glu Asn Val Asn Phe Thr Tyr Gln Glu Gly Thr
 1 5 10 15
 Pro Leu Ala Ser Ala Ala Leu Ser Asp Val Ser Leu Thr Ile Glu Asp
 20 25 30
 50 Gly Ser Tyr Thr Ala Leu Ile Gly His Thr Gly Ser Gly Lys Ser Thr
 35 40 45
 55 Ile Leu Gln Leu Leu Asn Gly Leu Leu Val Pro Ser Gln Gly Ser Val
 50 55 60
 Arg Val Phe Asp Thr Leu Ile Thr Ser Thr Ser Lys Asn Lys Asp Ile

	65		70		75		80									
	Arg	Gln	Ile	Arg	Lys	Gln	Val	Gly	Leu	Val	Phe	Gln	Phe	Ala	Glu	Asn
					85					90					95	
5	Gln	Ile	Phe	Glu	Glu	Thr	Val	Leu	Lys	Asp	Val	Ala	Phe	Gly	Pro	Gln
				100					105					110		
10	Asn	Phe	Gly	Val	Ser	Glu	Glu	Asp	Ala	Val	Lys	Thr	Ala	Arg	Glu	Lys
			115					120					125			
	Leu	Ala	Leu	Val	Gly	Ile	Asp	Glu	Ser	Leu	Phe	Asp	Arg	Ser	Pro	Phe
		130					135					140				
15	Glu	Leu	Ser	Gly	Gly	Gln	Met	Arg	Arg	Val	Ala	Ile	Ala	Gly	Ile	Leu
	145					150					155					160
	Ala	Met	Glu	Pro	Ala	Ile	Leu	Val	Leu	Asp	Glu	Pro	Thr	Ala	Gly	Leu
					165					170					175	
20	Asp	Pro	Leu	Gly	Arg	Lys	Glu	Leu	Met	Thr	Leu	Phe	Lys	Lys	Leu	His
				180					185					190		
25	Gln	Ser	Gly	Met	Thr	Ile	Val	Leu	Val	Thr	His	Leu	Met	Asp	Asp	Val
			195					200					205			
	Ala	Glu	Tyr	Ala	Asn	Gln	Val	Tyr	Val	Met	Glu	Lys	Gly	Arg	Leu	Val
		210					215					220				
30	Lys	Gly	Gly	Lys	Pro	Ser	Asp	Val	Phe	Gln	Asp	Val	Val	Phe	Met	Glu
	225					230					235					240
	Glu	Val	Gln	Leu	Gly	Val	Pro	Lys	Ile	Thr	Ala	Phe	Cys	Lys	Arg	Leu
				245						250					255	
35	Ala	Asp	Arg	Gly	Val	Ser	Phe	Lys	Arg	Leu	Pro	Val	Lys	Ile	Glu	Glu
				260					265					270		
40	Phe	Lys	Glu	Ser	Leu	Asn	Gly									
			275													
	<210>	129														
	<211>	309														
45	<212>	PRT														
	<213>	Streptococcus pneumoniae														
	<400>	129														
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	1				5					10					15	
	Arg	Asn	Val	Ser	Ser	Leu	Ala	Leu	Lys	Leu	Leu	Asp	Glu	Ile	Asn	Glu
				20					25					30		
55	Val	Trp	Leu	Phe	Asp	Cys	Gly	Glu	Gly	Thr	Gln	Asn	Arg	Ile	Leu	Glu
			35					40					45			

Thr Thr Ile Arg Pro Arg Lys Val Ser Lys Ile Phe Ile Thr His Leu
 50 55 60
 5 His Gly Asp His Ile Phe Gly Leu Pro Gly Phe Leu Ser Ser Arg Ala
 65 70 75 80
 Phe Gln Ala Asn Glu Glu Gln Thr Asp Leu Glu Ile Tyr Gly Pro Gln
 85 90 95
 10 Gly Ile Lys Ser Phe Val Leu Thr Ser Leu Arg Val Ser Gly Ser Arg
 100 105 110
 Leu Pro Tyr Arg Ile His Phe His Glu Phe Asp Gln Asp Ser Leu Gly
 115 120 125
 15 Lys Ile Leu Glu Ile Asp Lys Phe Thr Val Tyr Ala Glu Glu Leu Asp
 130 135 140
 His Thr Ile Phe Cys Val Gly Tyr Arg Val Met Gln Lys Asp Leu Glu
 145 150 155 160
 Gly Thr Leu Asp Ala Glu Lys Leu Lys Ala Ala Gly Val Pro Phe Gly
 165 170 175
 25 Pro Leu Phe Gly Lys Ile Lys Asn Gly Gln Asp Leu Val Leu Glu Asp
 180 185 190
 Gly Thr Glu Ile Lys Ala Ala Asp Tyr Ile Ser Ala Pro Arg Pro Gly
 195 200 205
 30 Lys Ile Ile Thr Ile Leu Gly Asp Thr Arg Lys Thr Asp Ala Ser Val
 210 215 220
 Arg Leu Ala Val Asn Ala Asp Val Leu Val His Glu Ser Thr Tyr Gly
 225 230 235 240
 Lys Gly Asp Glu Lys Ile Ala Arg Asn His Gly His Ser Thr Asn Met
 245 250 255
 40 Gln Ala Ala Gln Val Ala Val Glu Ala Gly Ala Lys Arg Leu Leu Leu
 260 265 270
 Asn His Ile Ser Ala Arg Phe Leu Ser Lys Asp Ile Ser Lys Leu Lys
 275 280 285
 45 Lys Asp Ala Ala Thr Ile Phe Glu Asn Val His Val Val Lys Asp Leu
 290 295 300
 Glu Glu Val Glu Ile
 50 305

<210> 130

<211> 553

<212> PRT

<213> Streptococcus pneumoniae

<400> 130
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 5 Lys Asn Met Tyr Ile Ala Glu Ile Gly Glu Ser Ile Phe Val Leu Asn
 20 25 30
 Val Gly Leu Lys Tyr Pro Glu Asn Glu Gln Leu Gly Val Asp Val Val
 35 40 45
 10 Ile Pro Asn Met Asp Tyr Leu Phe Glu Asn Ser Asp Arg Ile Ala Gly
 50 55 60
 15 Val Phe Leu Thr His Gly His Ala Asp Ala Ile Gly Ala Leu Pro Tyr
 65 70 75 80
 Leu Leu Ala Glu Ala Lys Val Pro Val Phe Gly Ser Glu Leu Thr Ile
 85 90 95
 20 Glu Leu Ala Lys Leu Phe Val Lys Gly Asn Asp Ala Val Lys Lys Phe
 100 105 110
 Asn Asp Phe His Val Ile Asp Glu Asn Thr Glu Ile Asp Phe Gly Gly
 115 120 125
 25 Thr Val Val Ser Phe Phe Pro Thr Thr Tyr Ser Val Pro Glu Ser Leu
 130 135 140
 30 Gly Ile Val Leu Lys Thr Ser Glu Gly Ser Ile Val Tyr Thr Gly Asp
 145 150 155 160
 Phe Lys Phe Asp Gln Thr Ala Ser Glu Ser Tyr Ala Thr Asp Phe Ala
 165 170 175
 35 Arg Leu Ala Glu Ile Gly Arg Asp Gly Val Leu Ala Leu Leu Ser Asp
 180 185 190
 Ser Ala Asn Ala Asp Ser Asn Ile Gln Val Ala Ser Glu Ser Glu Val
 195 200 205
 40 Arg Asp Glu Ile Thr Gln Thr Ile Ala Asp Trp Glu Gly Arg Ile Ile
 210 215 220
 Val Ala Ala Val Ser Ser Asn Leu Ser Arg Ile Gln Gln Ile Phe Asp
 225 230 235 240
 Ala Ala Asp Lys Thr Gly Arg Arg Ile Val Leu Thr Gly Phe Asp Ile
 245 250 255
 50 Glu Asn Ile Val Arg Thr Ala Ile Arg Leu Lys Lys Leu Ser Leu Ala
 260 265 270
 Asn Glu Ile Leu Leu Ile Lys Pro Lys Asp Met Ser Arg Phe Glu Asp
 275 280 285
 55 His Glu Leu Ile Ile Leu Glu Thr Gly Arg Met Gly Glu Pro Ile Asn
 290 295 300

Gly Leu Arg Lys Met Ser Ile Gly Arg His Arg Tyr Val Glu Ile Lys
 305 310 315 320
 5 Asp Gly Asp Leu Val Tyr Ile Ala Thr Ala Pro Ser Ile Ala Lys Glu
 325 330 335
 Ala Phe Val Ala Arg Val Glu Asn Met Ile Tyr Gln Ala Gly Gly Val
 340 345 350
 10 Val Lys Leu Ile Thr Gln Ser Leu His Val Ser Gly His Gly Asn Val
 355 360 365
 Arg Asp Leu Gln Leu Met Ile Asn Leu Leu Gln Pro Lys Tyr Leu Phe
 370 375 380
 15 Pro Val Gln Gly Glu Tyr Arg Glu Leu Asp Ala His Ala Lys Ala Ala
 385 390 395 400
 20 Met Ala Val Gly Met Leu Pro Glu Arg Ile Phe Ile Pro Lys Lys Gly
 405 410 415
 Thr Thr Met Ala Tyr Glu Asn Gly Asp Phe Val Pro Ala Gly Ser Val
 420 425 430
 25 Ser Ala Gly Asp Ile Leu Ile Asp Gly Asn Ala Ile Gly Asp Val Gly
 435 440 445
 Asn Val Val Leu Arg Asp Arg Lys Val Leu Ser Glu Asp Gly Ile Phe
 450 455 460
 Ile Val Ala Ile Thr Val Asn Arg Arg Glu Lys Lys Ile Val Ala Arg
 465 470 475 480
 35 Ala Arg Val His Thr Arg Gly Phe Val Tyr Leu Lys Lys Ser Arg Asp
 485 490 495
 Ile Leu Arg Glu Ser Ser Glu Leu Ile Asn Gln Thr Val Glu Asp Tyr
 500 505 510
 40 Leu Gln Gly Asp Asp Phe Asp Trp Ala Asp Leu Lys Gly Lys Val Arg
 515 520 525
 Asp Asn Leu Thr Lys Tyr Leu Phe Asp Gln Thr Lys Arg Arg Pro Ala
 530 535 540
 45 Ile Leu Pro Val Val Met Glu Ala Lys
 545 550
 50 <210> 131
 <211> 316
 <212> PRT
 <213> Streptococcus pneumoniae
 55 <400> 131
 Met Thr Lys Glu Phe His His Val Thr Val Leu Leu His Glu Thr Ile

	1		5		10		15									
	Asp	Met	Leu	Asp	Val	Lys	Pro	Asp	Gly	Ile	Tyr	Val	Asp	Ala	Thr	Leu
			20						25					30		
5	Gly	Gly	Ala	Gly	His	Ser	Glu	Tyr	Leu	Leu	Ser	Lys	Leu	Ser	Glu	Lys
			35					40					45			
	Gly	His	Leu	Tyr	Ala	Phe	Asp	Gln	Asp	Gln	Asn	Ala	Ile	Asp	Asn	Ala
10		50					55					60				
	Gln	Lys	Arg	Leu	Ala	Pro	Tyr	Ile	Glu	Lys	Gly	Val	Val	Thr	Phe	Ile
	65					70					75					80
15	Lys	Asp	Asn	Phe	Arg	His	Leu	Gln	Ala	Arg	Leu	Arg	Glu	Ala	Gly	Val
				85						90					95	
	Gln	Glu	Ile	Asp	Gly	Ile	Cys	Tyr	Asp	Leu	Gly	Val	Ser	Ser	Pro	Gln
20			100						105					110		
	Leu	Asp	Gln	Arg	Glu	Arg	Gly	Phe	Ser	Tyr	Lys	Lys	Asp	Ala	Pro	Leu
		115						120					125			
25	Asp	Met	Arg	Met	Asn	Gln	Asp	Ala	Ser	Leu	Thr	Ala	Tyr	Glu	Val	Val
	130						135					140				
	Asn	His	Tyr	Asp	Tyr	His	Asp	Leu	Val	Arg	Ile	Phe	Phe	Lys	Tyr	Gly
	145					150					155					160
30	Glu	Asp	Lys	Phe	Ser	Lys	Gln	Ile	Ala	Arg	Lys	Ile	Glu	Gln	Ala	Arg
				165						170					175	
	Glu	Val	Lys	Pro	Ile	Glu	Thr	Thr	Thr	Glu	Leu	Ala	Glu	Ile	Ile	Lys
35			180						185					190		
	Leu	Val	Lys	Pro	Ala	Lys	Glu	Leu	Lys	Lys	Lys	Gly	His	Pro	Ala	Lys
		195						200					205			
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	Ala	Asp	Glu	Ser	Ile	Gln	Gln	Ala	Met	Asp	Met	Leu	Ala	Leu	Asp	Gly
	225					230				235					240	
45	Arg	Ile	Ser	Val	Ile	Thr	Phe	His	Ser	Leu	Glu	Asp	Arg	Leu	Thr	Lys
				245						250					255	
	Gln	Leu	Phe	Lys	Glu	Ala	Ser	Thr	Val	Glu	Val	Pro	Lys	Gly	Leu	Pro
			260						265					270		
50	Phe	Ile	Pro	Asp	Asp	Leu	Lys	Pro	Lys	Met	Glu	Leu	Val	Ser	Arg	Lys
		275						280					285			
55	Pro	Ile	Leu	Pro	Ser	Ala	Glu	Glu	Leu	Glu	Ala	Asn	Asn	Arg	Ser	His
	290						295					300				
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Gly Leu Asp Tyr Val Asp Gln Lys Ile Leu Arg Thr Met Ile Glu Met
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 5 Tyr Ser Gly Gly Pro Val Gly Leu Gly Thr Leu Ser Val Asn Ile Ala
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 Glu Glu Arg Glu Thr Val Glu Asp Met Tyr Glu Pro Tyr Leu Ile Gln
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 35 40 45
 Val Val Asp Glu Gly Leu Arg Thr Leu Met Asp Phe Arg Tyr Asn Arg
 50 55 60
 35 His Phe Lys Ala Asp Ser Gly Glu Lys Gly Met Thr Lys Gly Met His
 65 70 75 80
 Gly Arg Gly Ala Glu Asp Leu Arg Val Arg Val Ser Gln Gly Thr Thr
 85 90 95
 40 Val Arg Asp Ala Glu Thr Gly Lys Val Leu Thr Asp Leu Ile Lys His
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 45 Gly Gln Glu Phe Ile Val Ala His Gly Gly Arg Gly Gly Arg Gly Asn
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 Ile Arg Phe Ala Thr Pro Lys Asn Pro Ala Pro Glu Ile Ser Glu Asn
 130 135 140
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 Ala Asp Val Gly Leu Val Gly Phe Pro Ser Val Gly Lys Ser Thr Leu
 165 170 175
 55 Leu Ser Val Ile Thr Ser Ala Lys Pro Lys Ile Gly Ala Tyr His Phe
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	225					230					235					240
10	Val	Ile	Leu	His	Ile	Ile	Asp	Met	Ser	Ala	Ser	Glu	Gly	Arg	Asp	Pro
				245						250					255	
	Tyr	Glu	Asp	Tyr	Leu	Ala	Ile	Asn	Lys	Glu	Leu	Glu	Ser	Tyr	Asn	Leu
15				260					265					270		
	Arg	Leu	Met	Glu	Arg	Pro	Gln	Ile	Ile	Val	Ala	Asn	Lys	Met	Asp	Met
			275					280					285			
20	Pro	Glu	Ser	Gln	Glu	Asn	Leu	Glu	Glu	Phe	Lys	Lys	Lys	Leu	Ala	Glu
	290						295					300				
	Asn	Tyr	Asp	Glu	Phe	Glu	Glu	Leu	Pro	Ala	Ile	Phe	Pro	Ile	Ser	Gly
	305					310					315					320
25	Leu	Thr	Lys	Gln	Gly	Leu	Ala	Thr	Leu	Leu	Asp	Ala	Thr	Ala	Glu	Leu
					325					330					335	
	Leu	Asp	Lys	Thr	Pro	Glu	Phe	Leu	Leu	Tyr	Asp	Glu	Ser	Asp	Met	Glu
30				340					345					350		
	Glu	Glu	Ala	Tyr	Tyr	Gly	Phe	Asp	Glu	Glu	Glu	Lys	Ala	Phe	Glu	Ile
			355					360					365			
35	Ser	Arg	Asp	Asp	Asp	Ala	Thr	Trp	Val	Leu	Ser	Gly	Glu	Lys	Leu	Met
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	Lys	Leu	Phe	Asn	Met	Thr	Asn	Phe	Asp	Arg	Asp	Glu	Ser	Val	Met	Lys
	385					390					395					400
40	Phe	Ala	Arg	Gln	Leu	Arg	Gly	Met	Gly	Val	Asp	Glu	Ala	Leu	Arg	Ala
					405					410					415	
	Arg	Gly	Ala	Lys	Asp	Gly	Asp	Leu	Val	Arg	Ile	Gly	Lys	Phe	Glu	Phe
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5	Lys	Lys	Gly	Ala	Glu	Leu	Ala	Leu	Phe	Asp	Glu	Lys	Asp	Gln	Phe	Val
			35					40					45			
	Gln	Thr	Val	Thr	Ile	Ala	Ser	His	Arg	Lys	Gln	Lys	Asn	Phe	Asp	Ile
10		50					55					60				
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15	Gly	Tyr	Ser	Leu	Lys	Val	Ala	Glu	Glu	Asp	Leu	Asn	Asp	Leu	Asp	Asp
					85					90					95	
	Gly	Glu	Phe	Tyr	Tyr	His	Glu	Ile	Ile	Gly	Leu	Glu	Val	Tyr	Glu	Gly
20				100					105					110		
	Asp	Ser	Leu	Val	Gly	Thr	Ile	Lys	Glu	Ile	Leu	Gln	Pro	Gly	Ala	Asn
			115					120					125			
25	Asp	Val	Trp	Val	Val	Lys	Arg	Lys	Gly	Lys	Arg	Asp	Leu	Leu	Leu	Pro
		130					135					140				
	Tyr	Ile	Pro	Pro	Val	Val	Leu	Asn	Val	Asp	Ile	Pro	Asn	Lys	Arg	Val
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	Glu	His	Ser	Ile	Val	Gly	Lys	Ala	Arg	Glu	Lys	Gly	Leu	Leu	Asp	Ile
45				20					25					30		
	Gln	Tyr	His	Asn	Phe	Arg	Glu	Asn	Ala	Glu	Lys	Ala	Arg	His	Val	Asp
			35					40					45			
50	Asp	Glu	Pro	Tyr	Gly	Gly	Gly	Gln	Gly	Met	Leu	Leu	Arg	Ala	Gln	Pro
		50					55					60				
	Ile	Phe	Asp	Ser	Phe	Asp	Ala	Ile	Glu	Lys	Lys	Asn	Pro	Arg	Val	Ile
	65					70					75					80
55	Leu	Leu	Asp	Pro	Ala	Gly	Lys	Gln	Phe	Asp	Gln	Ala	Tyr	Ala	Glu	Asp
					85					90					95	

Leu Ala Gln Glu Glu Glu Leu Ile Phe Ile Cys Gly His Tyr Glu Gly
 100 105 110
 5 Tyr Asp Glu Arg Ile Lys Thr Leu Val Thr Asp Glu Ile Ser Leu Gly
 115 120 125
 Asp Tyr Val Leu Thr Gly Gly Glu Leu Ala Ala Met Thr Met Ile Asp
 130 135 140
 10 Ala Thr Val Arg Leu Ile Pro Glu Val Ile Gly Lys Glu Ser Ser His
 145 150 155 160
 Gln Asp Asp Ser Phe Ser Ser Gly Leu Leu Glu Tyr His Gln Tyr Thr
 165 170 175
 15 Arg Pro Tyr Asp Tyr Arg Gly Met Val Val Pro Asp Val Leu Met Ser
 180 185 190
 20 Gly His His Glu Lys Ile Arg Gln Trp Arg Leu Tyr Glu Ser Leu Lys
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 Lys Thr Tyr Glu Arg Arg Pro Asp Leu Leu Glu His Tyr Gln Leu Thr
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 35 40 45
 Ser Thr Phe Asp Thr Ser Tyr Arg Pro Glu Glu Lys Phe Glu Gln Ala
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 Ile Ile Glu Thr Val Pro Ala Gln Tyr Leu Tyr Lys Met Asp Asp Thr
 65 70 75 80
 55 Ala Tyr Phe Met Asn Thr Glu Thr Tyr Asp Gln Tyr Glu Ile Pro Val
 85 90 95
 Val Asn Val Glu Asn Glu Leu Leu Tyr Ile Leu Glu Asn Ser Asp Val

	100	105	110
	Lys Ile Gln Phe Tyr Gly Thr Glu Val Ile Gly Val Thr Val Pro Thr		
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5	Thr Val Glu Leu Thr Val Ala Glu Thr Gln Pro Ser Ile Lys Gly Ala		
	130	135	140
	Thr Val Thr Gly Ser Gly Lys Pro Ala Thr Met Glu Thr Gly Leu Val		
10	145	150	155
	Val Asn Val Pro Asp Phe Ile Glu Ala Gly Gln Lys Leu Val Ile Asn		
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	180	185	
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	Lys Glu Ile Arg Leu Ala Leu Leu Glu Ala Asp Val Ala Leu Pro Val		
	35	40	45
35	Val Lys Asp Phe Ile Lys Lys Val Arg Glu Arg Ala Val Gly His Glu		
	50	55	60
	Val Ile Asp Thr Leu Asn Pro Ala Gln Gln Ile Ile Lys Ile Val Asp		
	65	70	75
40	Glu Glu Leu Thr Ala Val Leu Gly Ser Asp Thr Ala Glu Ile Ile Lys		
	85	90	95
	Ser Pro Lys Ile Pro Thr Ile Ile Met Met Val Gly Leu Gln Gly Ala		
45	100	105	110
	Gly Lys Thr Thr Phe Ala Gly Lys Leu Ala Asn Lys Leu Lys Lys Glu		
	115	120	125
50	Glu Asn Ala Arg Pro Leu Met Ile Ala Ala Asp Ile Tyr Arg Pro Ala		
	130	135	140
	Ala Ile Asp Gln Leu Lys Thr Leu Gly Gln Gln Ile Asp Val Pro Val		
	145	150	155
55	Phe Ala Leu Gly Thr Glu Val Pro Ala Val Glu Ile Val Arg Gln Gly		
	165	170	175

	Leu	Glu	Gln	Ala	Gln	Thr	Asn	His	Asn	Asp	Tyr	Val	Leu	Ile	Asp	Thr	
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5	Ala	Gly	Arg	Leu	Gln	Ile	Asp	Glu	Leu	Leu	Met	Asn	Glu	Leu	Arg	Asp	
			195					200					205				
	Val	Lys	Thr	Leu	Ala	Gln	Pro	Asn	Glu	Ile	Leu	Leu	Val	Val	Asp	Ala	
		210					215					220					
10	Met	Ile	Gly	Gln	Glu	Ala	Ala	Asn	Val	Ala	Arg	Glu	Phe	Asn	Ala	Gln	
	225					230					235					240	
	Leu	Glu	Val	Thr	Gly	Val	Ile	Leu	Thr	Lys	Ile	Asp	Gly	Asp	Thr	Arg	
15					245					250					255		
	Gly	Gly	Ala	Ala	Leu	Ser	Val	Arg	His	Ile	Thr	Gly	Lys	Pro	Ile	Lys	
				260					265					270			
20	Phe	Thr	Gly	Thr	Gly	Glu	Lys	Ile	Thr	Asp	Ile	Glu	Thr	Phe	His	Pro	
			275					280					285				
	Asp	Arg	Met	Ser	Ser	Arg	Ile	Leu	Gly	Met	Gly	Asp	Met	Leu	Thr	Leu	
25		290					295					300					
	Ile	Glu	Lys	Ala	Ser	Gln	Glu	Tyr	Asp	Glu	Gln	Lys	Ala	Leu	Glu	Met	
	305					310					315					320	
	Ala	Glu	Lys	Met	Arg	Glu	Asn	Thr	Phe	Asp	Phe	Asn	Asp	Phe	Ile	Asp	
30					325					330					335		
	Gln	Leu	Asp	Gln	Val	Gln	Asn	Met	Gly	Pro	Met	Glu	Asp	Leu	Leu	Lys	
				340					345					350			
35	Met	Ile	Pro	Gly	Met	Ala	Asn	Asn	Pro	Ala	Leu	Gln	Asn	Met	Lys	Val	
			355					360					365				
	Asp	Glu	Arg	Gln	Ile	Ala	Arg	Lys	Arg	Ala	Ile	Val	Ser	Ser	Met	Thr	
40		370					375					380					
	Pro	Glu	Glu	Arg	Glu	Asn	Pro	Asp	Leu	Leu	Asn	Pro	Ser	Arg	Arg	Arg	
	385					390					395					400	
	Arg	Ile	Ala	Ala	Gly	Ser	Gly	Asn	Thr	Phe	Val	Glu	Val	Asn	Lys	Phe	
45					405					410					415		
	Ile	Lys	Asp	Phe	Asn	Gln	Ala	Lys	Gln	Leu	Met	Gln	Gly	Val	Met	Ser	
				420					425					430			
50	Gly	Asp	Met	Asn	Lys	Met	Met	Lys	Gln	Met	Gly	Ile	Asn	Pro	Asn	Asn	
			435					440					445				
	Leu	Pro	Lys	Asn	Met	Pro	Asn	Met	Gly	Gly	Met	Asp	Met	Ser	Ala	Leu	
55				450			455					460					
	Glu	Gly	Met	Met	Gly	Gln	Gly	Gly	Met	Pro	Asp	Leu	Ser	Ala	Leu	Gly	
	465					470					475					480	

Position	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
	Gly	Ala	Gly	Met	Pro	Asp	Met	Ser	Gln	Met	Phe	Gly	Gly	Gly	Leu	Lys		
					485					490					495			
5	Gly	Lys	Ile	Gly	Glu	Phe	Ala	Met	Lys	Gln	Ser	Met	Lys	Arg	Met	Ala		
				500					505					510				
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			515					520										
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	1				5					10					15			
20	Gly	Ile	Thr	Glu	Trp	Leu	Pro	Ile	Ser	Ser	Thr	Gly	His	Leu	Ile	Leu		
				20					25					30				
	Ala	Glu	Glu	Phe	Ile	Gln	Tyr	Gln	Asn	Gln	Asn	Glu	Ala	Phe	Met	Ser		
25			35					40					45					
	Met	Phe	Asn	Val	Val	Ile	Gln	Leu	Gly	Ala	Ile	Leu	Ala	Val	Met	Val		
		50					55					60						
30	Ile	Tyr	Phe	Asn	Lys	Leu	Asn	Pro	Phe	Lys	Pro	Thr	Lys	Asp	Lys	Gln		
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	Glu	Val	Arg	Lys	Thr	Trp	Arg	Leu	Trp	Leu	Lys	Val	Leu	Ile	Ala	Thr		
					85					90					95			
35	Leu	Pro	Leu	Leu	Gly	Val	Phe	Lys	Phe	Asp	Asp	Trp	Phe	Asp	Thr	His		
				100					105					110				
	Phe	His	Asn	Met	Val	Ser	Val	Ala	Leu	Met	Leu	Ile	Ile	Tyr	Gly	Val		
40			115					120					125					
	Ala	Phe	Ile	Tyr	Leu	Glu	Lys	Arg	Asn	Lys	Ala	Arg	Ala	Ile	Glu	Pro		
		130					135					140						
45	Ser	Val	Thr	Glu	Leu	Asp	Lys	Leu	Pro	Tyr	Thr	Thr	Ala	Phe	Tyr	Ile		
	145					150					155					160		

	210	215	220
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	Ser Met Val Ala Ile Arg Phe Leu Thr Ser Tyr Val Lys Lys His Asp 245 250 255		
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30	Glu Val Glu Ser Ser Glu Glu Ser Val Phe Gln Glu Glu Asp Ser Gln 50 55 60		
35	Asp Thr Val Glu Glu Asn Leu Asp Leu Glu Pro Val Val Glu Val Ser 65 70 75 80		
	Gln Glu Glu Val Glu Glu Phe Pro Asn Ser Gln Glu Val Thr Glu Glu 85 90 95		
40	Glu Lys Leu Glu His Glu Gly Thr Val Glu Glu Asn Asn Phe Glu Val 100 105 110		
	Leu Glu Pro Glu Ala Pro Gln Thr Glu Glu Thr Val Gln Glu Lys Tyr 115 120 125		
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50	Ala Phe Phe Ala Asn Phe Arg Ser Val Asp Glu Glu Phe Phe Glu Glu 145 150 155 160		
	Leu Glu Glu Leu Leu Ile Met Ser Asp Val Gly Val Gln Val Ala Ser 165 170 175		
55	Asn Leu Thr Glu Glu Leu Arg Tyr Glu Ala Lys Leu Glu Asn Ala Lys 180 185 190		

Lys Pro Asp Ala Leu Arg Arg Val Il Ile Glu Lys Leu Val Glu Leu
 195 200 205
 5 Tyr Glu Lys Asp Gly Ser Tyr Asp Glu Ser Ile His Phe Gln Asp Asn
 210 215 220
 Leu Thr Val Met Leu Phe Val Gly Val Asn Gly Val Gly Lys Thr Thr
 225 230 235 240
 10 Ser Ile Gly Lys Leu Ala His Arg Tyr Lys Arg Ala Gly Lys Lys Val
 245 250 255
 Met Leu Val Ala Ala Asp Thr Phe Arg Ala Gly Ala Val Ala Gln Leu
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 15 Ala Glu Trp Gly Arg Arg Val Asp Val Pro Val Val Thr Gly Pro Glu
 275 280 285
 20 Lys Ala Asp Pro Ala Ser Val Val Phe Asp Gly Met Glu Arg Ala Val
 290 295 300
 Ala Glu Gly Ile Asp Ile Leu Met Ile Asp Thr Ala Gly Arg Leu Gln
 305 310 315 320
 25 Asn Lys Asp Asn Leu Met Ala Glu Leu Glu Lys Ile Gly Arg Ile Ile
 325 330 335
 Lys Arg Val Val Pro Glu Ala Pro His Glu Thr Phe Leu Ala Leu Asp
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 30 Ala Ser Thr Gly Gln Asn Ala Leu Val Gln Ala Lys Glu Phe Ser Lys
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 35 Ile Thr Pro Leu Thr Gly Ile Val Leu Thr Lys Ile Asp Gly Thr Ala
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 35 40 45
 5 His Glu Leu Asn Leu Glu Tyr Arg Asp Thr Asp Arg Pro Thr Asp Val
 50 55 60
 Ile Ser Leu Glu Tyr Lys Pro Glu Leu Glu Ile Ala Phe Asp Glu Glu
 65 70 75 80
 10 Asp Leu Leu Glu Asn Pro Glu Leu Ala Glu Met Met Ser Glu Phe Asp
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 Ala Tyr Ile Gly Glu Leu Phe Ile Ser Ile Asp Lys Ala His Glu Gln
 100 105 110
 15 Ala Glu Glu Tyr Gly His Ser Phe Glu Arg Glu Met Gly Phe Leu Ala
 115 120 125
 20 Val His Gly Phe Leu His Ile Asn Gly Tyr Asp His Tyr Thr Pro Glu
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 35 40 45
 45 Phe Lys Asp Lys Ala Asp Leu Ala Gly Phe Glu Ala Asp Val Trp Val
 50 55 60
 Asp Phe Thr Thr Pro Ala Val Ala Tyr Glu Asn Thr Arg Phe Ala Leu
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 50 Glu Asn Gly Phe Ala Pro Val Val Gly Thr Thr Gly Phe Thr Ser Glu
 85 90 95
 55 Glu Ile Ala Glu Leu Lys Glu Phe Ser Arg Ala Gln Asp Leu Gly Gly
 100 105 110
 Leu Ile Ala Pro Asn Phe Ala Leu Gly Ala Val Leu Leu Met Gln Phe

	115	120	125
5	Ala Thr Gln Ala Ala Lys Tyr Phe Pro Asn Val Glu Ile Ile Glu Leu 130	135	140
	His His Asp Lys Lys Lys Asp Ala Pro Ser Gly Thr Ala Ile Lys Thr 145	150	155 160
10	Ala Glu Leu Met Ala Glu Val Arg Glu Ser Ile Gln Gln Gly Ala Ala 165	170	175
	Asp Glu Glu Glu Leu Ile Ala Gly Ala Arg Gly Ala Asp Phe Asp Gly 180	185	190
15	Met Arg Ile His Ser Val Arg Leu Pro Gly Leu Val Ala His Gln Glu 195	200	205
20	Val Ile Phe Gly Asn Gln Gly Glu Gly Leu Thr Leu Arg His Asp Ser 210	215	220
	Tyr Asp Arg Ile Ser Phe Met Thr Gly Val Asn Leu Gly Ile Lys Glu 225	230	235 240
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45	Val Ala Asp Tyr Leu Ala Ala Gly Glu Lys Val Gln Leu Ile Gly Phe 35 40 45		
50	Ser Asn Phe Glu Val Arg Glu Arg Ala Glu Arg Lys Gly Arg Asn Pro 50 55 60		
55	Gln Thr Gly Lys Glu Met Thr Ile Ala Ala Ser Lys Val Pro Ala Phe 65 70 75 80		
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				20					25					30		
	Ile	Asp	Arg	Ala	Ser	Gln	Val	Leu	Gly	Tyr	Asp	Leu	Arg	Tyr	Leu	Ile
			35					40					45			
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		50					55					60				
	Ile	Leu	Ala	Thr	Ser	Val	Ala	Ile	Tyr	Arg	Leu	Leu	Gln	Glu	Lys	Gly
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	Tyr	Gln	Pro	Asp	Met	Val	Ala	Gly	Leu	Ser	Leu	Gly	Glu	Tyr	Ser	Ala
					85					90					95	
20	Leu	Val	Ala	Ser	Gly	Ala	Leu	Asp	Phe	Glu	Asp	Ala	Val	Ala	Leu	Val
				100					105					110		
	Ala	Lys	Arg	Gly	Ala	Tyr	Met	Glu	Glu	Ala	Ala	Pro	Ala	Asp	Ser	Gly
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	Lys	Met	Val	Ala	Val	Leu	Asn	Thr	Pro	Val	Glu	Val	Ile	Glu	Glu	Ala
		130					135					140				
	Cys	Gln	Lys	Ala	Ser	Glu	Leu	Gly	Val	Val	Thr	Pro	Ala	Asn	Tyr	Asn
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	Thr	Pro	Ala	Gln	Ile	Val	Ile	Ala	Gly	Glu	Val	Val	Ala	Val	Asp	Arg
					165					170					175	
35	Ala	Val	Glu	Leu	Leu	Gln	Glu	Ala	Gly	Ala	Lys	Arg	Leu	Ile	Pro	Leu
				180					185					190		
	Lys	Val	Ser	Gly	Pro	Phe	His	Thr	Ala	Leu	Leu	Glu	Pro	Ala	Ser	Gln
			195					200					205			
40	Lys	Leu	Ala	Glu	Thr	Leu	Ala	Gln	Val	Ser	Phe	Ser	Asp	Phe	Thr	Cys
		210					215					220				
	Pro	Leu	Val	Gly	Asn	Thr	Glu	Ala	Ala	Val	Met	Gln	Lys	Glu	Asp	Ile
45	225					230					235					240
	Ala	Gln	Leu	Leu	Thr	Arg	Gln	Val	Lys	Glu	Pro	Val	Arg	Phe	Tyr	Glu
					245					250					255	
50	Ser	Ile	Gly	Val	Met	Gln	Glu	Ala	Gly	Ile	Ser	Asn	Phe	Ile	Glu	Ile
				260					265					270		
	Gly	Pro	Gly	Lys	Val	Leu	Ser	Gly	Phe	Val	Lys	Lys	Ile	Asp	Gln	Thr
			275					280					285			
55	Ala	His	Leu	Ala	His	Val	Glu	Asp	Gln	Ala	Ser	Leu	Val	Ala	Leu	Leu
		290					295					300				

Glu Lys
305

5

<210> 144
<211> 243
<212> PRT
<213> Streptococcus pneumoniae

10

<400> 144
Met Lys Leu Glu His Lys Asn Ile Phe Ile Thr Gly Ser Ser Arg Gly
1 5 10 15

15

Ile Gly Leu Ala Ile Ala His Lys Phe Ala Gln Ala Gly Ala Asn Ile
20 25 30

Val Leu Asn Ser Arg Gly Ala Ile Ser Glu Glu Leu Leu Ala Glu Phe
35 40 45

20

Ser Asn Tyr Gly Ile Lys Val Val Pro Ile Ser Gly Asp Val Ser Asp
50 55 60

25

Phe Ala Asp Ala Lys Arg Met Ile Asp Gln Ala Ile Ala Glu Leu Gly
65 70 75 80

Ser Val Asp Val Leu Val Asn Asn Ala Gly Ile Thr Gln Asp Thr Leu
85 90 95

30

Met Leu Lys Met Thr Glu Ala Asp Phe Glu Lys Val Leu Lys Val Asn
100 105 110

Leu Thr Gly Ala Phe Asn Met Thr Gln Ser Val Leu Lys Pro Met Met
115 120 125

35

Lys Ala Arg Glu Gly Ala Ile Ile Asn Met Ser Ser Val Val Gly Leu
130 135 140

40

Met Gly Asn Ile Gly Gln Ala Asn Tyr Ala Ala Ser Lys Ala Gly Leu
145 150 155 160

Ile Gly Phe Thr Lys Ser Val Ala Arg Glu Val Ala Ser Arg Asn Ile
165 170 175

45

Arg Val Asn Val Ile Ala Pro Gly Met Ile Glu Ser Asp Met Thr Ala
180 185 190

Ile Leu Ser Asp Lys Ile Lys Glu Ala Thr Leu Ala Gln Ile Pro Met
195 200 205

50

Lys Glu Phe Gly Gln Ala Glu Gln Val Ala Asp Leu Thr Val Phe Leu
210 215 220

55

Ala Gly Gln Asp Tyr Leu Thr Gly Gln Val Val Ala Ile Asp Gly Gly
225 230 235 240

Leu Ser Met

5 <210> 145
 <211> 276
 <212> PRT
 <213> Streptococcus pneumoniae

10 <400> 145
 Met Gly Val Lys Lys Lys Leu Lys Leu Thr Ser Leu Leu Gly Leu Ser
 1 5 10 15
 Leu Leu Ile Met Thr Ala Cys Ala Thr Asn Gly Val Thr Ser Asp Ile
 20 25 30
 15 Thr Ala Glu Ser Ala Asp Phe Trp Ser Lys Leu Val Tyr Phe Phe Ala
 35 40 45
 Glu Ile Ile Arg Phe Leu Ser Phe Asp Ile Ser Ile Gly Val Gly Ile
 20 50 55 60
 Ile Leu Phe Thr Val Leu Ile Arg Thr Val Leu Leu Pro Val Phe Gln
 65 70 75 80
 25 Val Gln Met Val Ala Ser Arg Lys Met Gln Glu Ala Gln Pro Arg Ile
 85 90 95
 Lys Ala Leu Arg Glu Gln Tyr Pro Gly Arg Asp Met Glu Ser Arg Thr
 100 105 110
 30 Lys Leu Glu Gln Glu Met Arg Lys Val Phe Lys Glu Met Gly Val Arg
 115 120 125
 Gln Ser Asp Ser Leu Trp Pro Ile Leu Ile Gln Met Pro Val Ile Leu
 35 130 135 140
 Ala Leu Phe Gln Ala Leu Ser Arg Val Asp Phe Leu Lys Thr Gly His
 145 150 155 160
 40 Phe Leu Trp Ile Asn Leu Gly Ser Val Asp Thr Thr Leu Val Leu Pro
 165 170 175
 Ile Leu Ala Ala Val Phe Thr Phe Leu Ser Thr Trp Leu Ser Asn Lys
 180 185 190
 45 Ala Leu Ser Glu Arg Asn Gly Ala Thr Thr Ala Met Met Tyr Gly Ile
 195 200 205
 Pro Val Leu Ile Phe Ile Phe Ala Val Tyr Ala Pro Gly Gly Val Ala
 50 210 215 220
 Leu Tyr Trp Thr Val Ser Asn Ala Tyr Gln Val Leu Gln Thr Tyr Phe
 225 230 235 240
 55 Leu Asn Asn Pro Phe Lys Ile Ile Ala Glu Arg Glu Ala Val Val Gln
 245 250 255

Ala Gln Lys Asp Leu Glu Asn Arg Lys Arg Lys Ala Lys Lys Lys Ala
 260 265 270

5 Gln Lys Thr Lys
 275

<210> 146

<211> 409

10 <212> PRT

<213> Streptococcus pneumoniae

<400> 146

15 Met Lys Ile Ser Lys Arg His Leu Leu Asn Tyr Ser Ile Leu Ile Pro
 1 5 10 15

Tyr Leu Leu Leu Ser Ile Leu Gly Leu Ile Val Val Tyr Ser Thr Thr
 20 25 30

20 Ser Ala Ile Leu Ile Glu Glu Gly Lys Ser Ala Leu Gln Leu Val Arg
 35 40 45

Asn Gln Gly Ile Phe Trp Ile Val Ser Leu Ile Leu Ile Ala Leu Ile
 50 55 60

25 Tyr Lys Leu Arg Leu Asp Phe Leu Arg Asn Glu Arg Leu Ile Ile Leu
 65 70 75 80

30 Val Ile Leu Ile Glu Met Leu Leu Leu Phe Leu Ala Arg Phe Ile Gly
 85 90 95

Ile Ser Val Asn Gly Ala Tyr Gly Trp Ile Ser Val Ala Gly Val Thr
 100 105 110

35 Ile Gln Pro Ala Glu Tyr Leu Lys Ile Ile Ile Ile Trp Tyr Leu Ala
 115 120 125

His Arg Phe Ser Lys Gln Gln Glu Glu Ile Ala Thr Tyr Asp Phe Gln
 130 135 140

40 Val Leu Thr Gln Asn Gln Trp Leu Pro Arg Ala Phe Asn Asp Trp Arg
 145 150 155 160

45 Phe Val Leu Leu Val Leu Ile Gly Ser Leu Gly Ile Phe Pro Asp Leu
 165 170 175

Gly Asn Ala Thr Ile Leu Val Leu Val Ser Leu Ile Met Tyr Thr Val
 180 185 190

50 Ser Gly Ile Ala Tyr Arg Trp Phe Ser Thr Ile Leu Ala Leu Val Ser
 195 200 205

Ala Thr Ser Val Phe Val Leu Thr Thr Ile Ser Leu Ile Gly Val Glu
 210 215 220

55 Thr Phe Ser Lys Ile Pro Val Phe Gly Tyr Val Ala Lys Arg Phe Ser
 225 230 235 240

Ala Phe Phe Asn Pro Phe Ala Asp Arg Ala Asp Ala Gly His Gln Leu
 245 250 255
 5 Ala Asn Ser Tyr Phe Ala Met Val Asn Gly Gly Trp Phe Gly Leu Gly
 260 265 270
 Leu Gly Asn Ser Ile Glu Lys Arg Gly Tyr Leu Pro Glu Ala His Thr
 275 280 285
 10 Asp Phe Val Phe Ser Ile Val Ile Glu Glu Phe Gly Phe Val Gly Ala
 290 295 300
 Ser Leu Ile Leu Ala Leu Leu Phe Phe Met Ile Leu Arg Ile Ile Leu
 305 310 315 320
 Val Gly Ile Arg Ala Glu Asn Pro Phe Asn Ala Met Val Ala Leu Gly
 325 330 335
 20 Val Gly Gly Met Met Leu Val Gln Val Phe Val Asn Ile Gly Gly Ile
 340 345 350
 Ser Gly Leu Ile Pro Ser Thr Gly Val Thr Phe Pro Phe Leu Ser Gln
 355 360 365
 25 Gly Gly Asn Ser Leu Leu Val Leu Ser Val Ala Val Ala Phe Val Leu
 370 375 380
 Asn Ile Asp Ala Ser Glu Lys Arg Ala Lys Leu Tyr Arg Glu Leu Glu
 385 390 395 400
 Asn Gln Pro Met Asn Leu Leu Leu Lys
 405
 35 <210> 147
 <211> 419
 <212> PRT
 <213> Streptococcus pneumoniae
 40 <400> 147
 Met Leu Gly Ile Leu Thr Phe Ile Leu Val Phe Gly Ile Ile Val Val
 1 5 10 15
 45 Val His Glu Phe Gly His Phe Tyr Phe Ala Lys Lys Ser Gly Ile Leu
 20 25 30
 Val Arg Glu Phe Ala Ile Gly Met Gly Pro Lys Ile Phe Ala His Ile
 35 40 45
 50 Gly Lys Asp Gly Thr Ala Tyr Thr Ile Arg Ile Leu Pro Leu Gly Gly
 50 55 60
 Tyr Val Arg Met Ala Gly Trp Gly Asp Asp Thr Thr Glu Ile Lys Thr
 55 65 70 75 80
 Gly Thr Pro Val Ser Leu Thr Leu Ala Asp Asp Gly Lys Val Lys Arg

	85	90	95
	Ile Asn Leu Ser Gly Lys Lys Leu Asp Gln Thr Ala Leu Pro Met Gln		
5	100	105	110
	Val Thr Gln Phe Asp Phe Glu Asp Lys Leu Phe Ile Lys Gly Leu Val		
	115	120	125
10	Leu Glu Glu Glu Lys Thr Phe Ala Val Asp His Asp Ala Thr Val Val		
	130	135	140
	Glu Ala Asp Gly Thr Glu Val Arg Ile Ala Pro Leu Asp Val Gln Tyr		
	145	150	155
15	Gln Asn Ala Thr Ile Trp Gly Lys Leu Ile Thr Asn Phe Ala Gly Pro		
	165	170	175
	Met Asn Asn Phe Ile Leu Gly Val Val Val Phe Trp Val Leu Ile Phe		
20	180	185	190
	Met Gln Gly Gly Val Arg Asp Val Asp Thr Asn Gln Phe His Ile Met		
	195	200	205
25	Pro Gln Gly Ala Leu Ala Lys Val Gly Val Pro Glu Thr Ala Gln Ile		
	210	215	220
	Thr Lys Ile Gly Ser His Glu Val Ser Asn Trp Glu Ser Leu Ile Gln		
	225	230	235
30	Ala Val Glu Thr Glu Thr Lys Asp Lys Thr Ala Pro Thr Leu Asp Val		
	245	250	255
	Thr Ile Ser Glu Lys Gly Ser Asp Lys Gln Val Thr Val Thr Pro Glu		
35	260	265	270
	Asp Ser Gln Gly Arg Tyr Leu Leu Gly Val Gln Pro Gly Val Lys Ser		
	275	280	285
40	Asp Phe Leu Ser Met Phe Val Gly Gly Phe Thr Thr Ala Ala Asp Ser		
	290	295	300
	Ala Leu Arg Ile Leu Ser Ala Leu Lys Asn Leu Ile Phe Gln Pro Asp		
	305	310	315
45	Leu Asn Lys Leu Gly Gly Pro Val Ala Ile Phe Lys Ala Ser Ser Asp		
	325	330	335
	Ala Ala Lys Asn Gly Ile Glu Asn Ile Leu Tyr Phe Leu Ala Met Ile		
50	340	345	350
	Ser Ile Asn Ile Gly Ile Phe Asn Leu Ile Pro Ile Pro Ala Leu Asp		
	355	360	365
55	Gly Gly Lys Ile Val Leu Asn Ile Leu Glu Ala Ile Arg Arg Lys Pro		
	370	375	380
	Leu Lys Gln Glu Ile Glu Thr Tyr Val Thr Leu Ala Gly Val Val Ile		

	385		390		395		400
	Met Val Val Leu Met	Ile Ala Val Thr Trp	Asn Asp Ile Met Arg Leu				
	405		410			415	
5	Phe Phe Arg						
10	<210> 148						
	<211> 197						
	<212> PRT						
	<213> Streptococcus pneumoniae						
15	<400> 148						
	Met Tyr Ala Tyr Leu Lys Gly Ile Ile Thr Lys Ile Thr Ala Lys Tyr						
	1	5		10		15	
20	Ile Val Leu Glu Thr Asn Gly Ile Gly Tyr Ile Leu His Val Ala Asn						
	20		25			30	
	Pro Tyr Ala Tyr Ser Gly Gln Val Asn Gln Glu Ala Gln Ile Tyr Val						
	35	40		45			
25	His Gln Val Val Arg Glu Asp Ala His Leu Leu Tyr Gly Phe Arg Ser						
	50	55		60			
	Glu Asp Glu Lys Lys Leu Phe Leu Ser Leu Ile Ser Val Ser Gly Ile						
	65	70		75		80	
30	Gly Pro Val Ser Ala Leu Ala Ile Ile Ala Ala Asp Asp Asn Ala Gly						
	85		90			95	
	Leu Val Gln Ala Ile Glu Thr Lys Asn Ile Thr Tyr Leu Thr Lys Phe						
35	100		105			110	
	Pro Lys Ile Gly Lys Lys Thr Ala Gln Gln Met Val Leu Asp Leu Glu						
	115	120		125			
40	Gly Lys Val Val Val Ala Gly Asp Asp Leu Pro Ala Lys Val Ala Val						
	130	135		140			
	Gln Ala Ser Ala Glu Asn Gln Glu Leu Glu Glu Ala Met Glu Ala Met						
	145	150		155		160	
45	Leu Ala Leu Gly Tyr Lys Ala Thr Glu Leu Lys Lys Ile Lys Lys Phe						
	165		170			175	
	Phe Glu Gly Thr Thr Asp Thr Ala Glu Asn Tyr Ile Lys Ser Ala Leu						
50	180		185			190	
	Lys Met Leu Val Lys						
	195						
55	<210> 149						
	<211> 257						

<212> PRT

<213> Streptococcus pneumoniae

<400> 149

5 Met Lys Asn Asn Arg Ile Leu Ala Leu Ser Gly Asn Asp Ile Phe Ser
 1 5 10 15

 Gly Gly Gly Leu Ser Ala Asp Leu Ala Thr Tyr Thr Leu Asn Gly Leu
 20 25 30
 10 His Gly Phe Val Ala Val Thr Cys Leu Thr Ala Leu Thr Glu Lys Gly
 35 40 45

 Phe Glu Val Phe Pro Thr Asp Asp Thr Ile Phe Gln His Glu Leu Asp
 15 50 55 60

 Ser Leu Arg Asp Val Glu Phe Gly Gly Ile Lys Ile Gly Leu Leu Pro
 65 70 75 80

 20 Thr Val Ser Val Ala Glu Lys Ala Leu Asp Phe Ile Lys Gln Arg Pro
 85 90 95

 Gly Val Pro Val Val Leu Asp Pro Val Leu Val Cys Lys Glu Thr His
 100 105 110
 25 Asp Val Ala Val Ser Glu Leu Cys Gln Glu Leu Ile Arg Phe Phe Pro
 115 120 125

 Tyr Val Ser Val Ile Thr Pro Asn Leu Pro Glu Ala Glu Leu Leu Ser
 30 130 135 140

 Gly Gln Glu Ile Lys Thr Leu Glu Asp Met Lys Thr Ala Ala Gln Lys
 145 150 155 160

 35 Leu His Asp Leu Gly Ala Pro Ala Val Ile Ile Lys Gly Gly Asn Arg
 165 170 175

 Leu Ser Gln Asp Lys Ala Val Asp Val Phe Tyr Asp Gly Gln Thr Phe
 180 185 190
 40 Thr Ile Leu Glu Asn Pro Val Ile Gln Gly Gln Asn Ala Gly Ala Gly
 195 200 205

 Cys Thr Phe Ala Ser Ser Ile Ala Ser His Leu Val Lys Gly Asp Lys
 45 210 215 220

 Phe Leu Pro Ala Val Glu Ser Ser Lys Ala Phe Val Tyr Arg Ala Ile
 225 230 235 240

 50 Ala Gln Ala Asp Gln Tyr Gly Val Arg Gln Tyr Glu Ala Asn Lys Asn
 245 250 255

 Asn

55

<210> 150

<211> 412

<212> PRT

<213> Streptococcus pneumoniae

5 <400> 150

Met Ile Glu Thr Glu Lys Lys Glu Glu Arg Val Leu Leu Ile Gly Val
 1 5 10 15

10 Glu Leu Gln Gly Met Asp Ser Phe Asp Leu Ser Met Glu Glu Leu Ala
 20 25 30

Ser Leu Ala Lys Thr Ala Gly Ala Val Val Val Asp Ser Tyr Arg Gln
 35 40 45

15 Lys Arg Glu Lys Tyr Asp Ser Lys Thr Phe Val Gly Ser Gly Lys Leu
 50 55 60

Glu Glu Ile Ala Leu Met Val Asp Ala Glu Glu Ile Thr Thr Val Ile
 65 70 75 80

20 Val Asn Asn Arg Leu Thr Pro Arg Gln Asn Val Asn Leu Glu Glu Val
 85 90 95

25 Leu Gly Val Lys Val Ile Asp Arg Met Gln Leu Ile Leu Asp Ile Phe
 100 105 110

Ala Met Arg Ala Arg Ser His Glu Gly Lys Leu Gln Val His Leu Ala
 115 120 125

30 Gln Phe Lys Tyr Leu Leu Pro Arg Leu Val Gly Gln Gly Ile Met Leu
 130 135 140

Ser Arg Gln Ala Gly Gly Ile Gly Ser Arg Gly Pro Gly Glu Ser Gln
 145 150 155 160

35 Leu Glu Leu Asn Arg Arg Ser Val Arg Asn Gln Ile Thr Asp Ile Glu
 165 170 175

40 Arg Gln Leu Lys Val Val Glu Lys Asn Arg Ala Thr Val Arg Glu Lys
 180 185 190

Arg Leu Glu Ser Ser Thr Phe Lys Ile Gly Leu Ile Gly Tyr Thr Asn
 195 200 205

45 Ala Gly Lys Ser Thr Ile Met Asn Ile Leu Thr Ser Lys Thr Gln Tyr
 210 215 220

Glu Ala Asp Glu Leu Phe Ala Thr Leu Asp Ala Thr Thr Lys Ser Ile
 225 230 235 240

50 His Leu Gly Gly Asn Leu Gln Val Thr Leu Thr Asp Thr Val Gly Phe
 245 250 255

55 Ile Gln Asp Leu Pro Thr Glu Leu Val Ser Ser Phe Lys Ser Thr Leu
 260 265 270

Glu Glu Ser Lys His Val Asp Leu Leu Val His Val Ile Asp Ala Ser

	275	280	285
5	Asn Pro Tyr His Glu Glu His Glu Lys Thr Val Leu Ser Ile Met Lys 290 295 300		
	Asp Leu Asp Met Glu Asp Ile Pro His Leu Thr Leu Tyr Asn Lys Ala 305 310 315 320		
10	Asp Leu Val Glu Asp Phe Thr Pro Thr Gln Thr Pro Tyr Thr Leu Ile 325 330 335		
	Ser Ala Lys Ser Glu Asp Ser Arg Glu Asn Leu Gln Ala Leu Leu Leu 340 345 350		
15	Asp Lys Ile Lys Glu Ile Phe Glu Ala Phe Thr Leu Arg Val Pro Phe 355 360 365		
	Ser Lys Ser Tyr Lys Ile His Asp Leu Glu Ser Val Ala Ile Leu Glu 370 375 380		
20	Glu Arg Asp Tyr Gln Glu Asp Gly Glu Val Ile Thr Gly Tyr Ile Ser 385 390 395 400		
25	Glu Lys Asn Lys Trp Arg Leu Glu Glu Phe Tyr Asp 405 410		
30	<210> 151 <211> 160 <212> PRT <213> Streptococcus pneumoniae		
35	<400> 151 Met Ala Glu Lys Thr Tyr Pro Met Thr Leu Glu Glu Lys Glu Lys Leu 1 5 10 15		
	Glu Lys Glu Leu Glu Glu Leu Lys Leu Val Arg Arg Pro Glu Val Val 20 25 30		
40	Glu Arg Ile Lys Ile Ala Arg Ser Tyr Gly Asp Leu Ser Glu Asn Ser 35 40 45		
45	Glu Tyr Glu Ala Ala Lys Asp Glu Gln Ala Phe Val Glu Gly Gln Ile 50 55 60		
	Ser Ser Leu Glu Thr Lys Ile Arg Tyr Ala Glu Ile Val Asn Ser Asp 65 70 75 80		
50	Ala Val Ala Gln Asp Glu Val Ala Ile Gly Lys Thr Val Thr Ile Gln 85 90 95		
	Glu Ile Gly Glu Asp Glu Glu Glu Val Tyr Ile Ile Val Gly Ser Ala 100 105 110		
55	Gly Ala Asp Ala Phe Ala Gly Lys Val Ser Asn Glu Ser Pro Ile Gly 115 120 125		

Gln Ala Leu Ile Gly Lys Lys Thr Gly Asp Thr Ala Thr Ile Glu Thr
 130 135 140

5 Pro Val Gly Ser Tyr Asp Val Lys Ile Leu Lys Val Glu Lys Thr Ala
 145 150 155 160

10 <210> 152
 <211> 189
 <212> PRT
 <213> Streptococcus pneumoniae

15 <400> 152
 Met Thr Lys Leu Leu Val Gly Leu Gly Asn Pro Gly Asp Lys Tyr Phe
 1 5 10 15

20 Glu Thr Lys His Asn Val Gly Phe Met Leu Ile Asp Gln Leu Ala Lys
 20 25 30

Lys Gln Asn Val Thr Phe Thr His Asp Lys Ile Phe Gln Ala Asp Leu
 35 40 45

25 Ala Ser Phe Phe Leu Asn Gly Glu Lys Ile Tyr Leu Val Lys Pro Thr
 50 55 60

30 Thr Phe Met Asn Glu Ser Gly Lys Ala Val His Ala Leu Leu Thr Tyr
 65 70 75 80

Tyr Gly Leu Asp Ile Asp Asp Leu Leu Ile Ile Tyr Asp Asp Leu Asp
 85 90 95

35 Met Glu Val Gly Lys Ile Arg Leu Arg Ala Lys Gly Ser Ala Gly Gly
 100 105 110

His Asn Gly Ile Lys Ser Ile Ile Gln His Ile Gly Thr Gln Val Phe
 115 120 125

40 Asn Arg Val Lys Ile Gly Ile Gly Arg Pro Lys Asn Gly Met Ser Val
 130 135 140

Val His His Val Leu Ser Lys Phe Asp Arg Asp Glu Tyr Ile Gly Ile
 45 145 150 155 160

Leu Gln Ser Val Asp Lys Val Asp Asp Ser Val Asn Tyr Tyr Leu Gln
 165 170 175

50 Glu Lys Asn Phe Glu Lys Thr Met Gln Arg Tyr Asn Gly
 180 185

55 <210> 153
 <211> 283
 <212> PRT
 <213> Streptococcus pneumoniae

<400> 153

5 Met Ile Leu Ile Thr Gly Ala Asn Gly Gln Leu Gly Thr Glu Leu Arg
 1 5 10 15
 Tyr Leu Leu Asp Glu Arg Asn Glu Glu Tyr Val Ala Val Asp Val Ala
 20 25 30
 10 Lys Met Asp Ile Thr Asn Glu Glu Met Val Glu Lys Val Phe Glu Glu
 35 40 45
 Val Lys Pro Thr Leu Val Tyr His Cys Ala Ala Tyr Thr Ala Val Asp
 50 55 60
 15 Ala Ala Glu Asp Glu Gly Lys Glu Leu Asp Phe Ala Ile Asn Val Thr
 65 70 75 80
 Gly Thr Lys Asn Val Ala Lys Ala Ser Glu Lys His Gly Ala Thr Leu
 85 90 95
 20 Val Tyr Ile Ser Thr Asp Tyr Val Phe Asp Gly Lys Lys Pro Val Gly
 100 105 110
 Gln Glu Trp Glu Val Asp Asp Arg Pro Asp Pro Gln Thr Glu Tyr Gly
 115 120 125
 Arg Thr Lys Arg Met Gly Glu Glu Leu Val Glu Lys His Val Ser Asn
 130 135 140
 30 Phe Tyr Ile Ile Arg Thr Ala Trp Val Phe Gly Asn Tyr Gly Lys Asn
 145 150 155 160
 Phe Val Phe Thr Met Gln Asn Leu Ala Lys Thr His Lys Thr Leu Thr
 165 170 175
 35 Val Val Asn Asp Gln Tyr Gly Arg Pro Thr Trp Thr Arg Thr Leu Ala
 180 185 190
 Glu Phe Met Thr Tyr Leu Ala Glu Asn Arg Lys Glu Phe Gly Tyr Tyr
 195 200 205
 His Leu Ser Asn Asp Ala Thr Glu Asp Thr Thr Trp Tyr Asp Phe Ala
 210 215 220
 45 Val Glu Ile Leu Lys Asp Thr Asp Val Glu Val Lys Pro Val Asp Ser
 225 230 235 240
 Ser Gln Phe Pro Ala Lys Ala Lys Arg Pro Leu Asn Ser Thr Met Ser
 245 250 255
 50 Leu Ala Lys Ala Lys Ala Thr Gly Phe Val Ile Pro Thr Trp Gln Asp
 260 265 270
 55 Ala Leu Gln Glu Phe Tyr Lys Gln Glu Val Arg
 275 280

5 <210> 154
 <211> 407
 <212> PRT
 <213> Streptococcus pneumoniae

 <400> 154
 10 Met Lys Arg Ser Leu Asp Ser Arg Val Asp Tyr Ser Leu Leu Leu Pro
 1 5 10 15
 Val Phe Phe Leu Leu Val Ile Gly Val Val Ala Ile Tyr Ile Ala Val
 20 25 30
 15 Ser His Asp Tyr Pro Asn Asn Ile Leu Pro Ile Leu Gly Gln Gln Val
 35 40 45
 Ala Trp Ile Ala Leu Gly Leu Val Ile Gly Phe Val Val Met Leu Phe
 50 55 60
 20 Asn Thr Glu Phe Leu Trp Lys Val Thr Pro Phe Leu Tyr Ile Leu Gly
 65 70 75 80
 Leu Gly Leu Met Ile Leu Pro Ile Val Phe Tyr Asn Pro Ser Leu Val
 25 85 90 95
 Ala Ser Thr Gly Ala Lys Asn Trp Val Ser Ile Asn Gly Ile Thr Leu
 100 105 110
 30 Phe Gln Pro Ser Glu Phe Met Lys Ile Ser Tyr Ile Leu Met Leu Ala
 115 120 125
 Arg Val Ile Val Gln Phe Thr Lys Lys His Lys Glu Trp Arg Arg Thr
 130 135 140
 35 Val Pro Leu Asp Phe Leu Leu Ile Phe Trp Met Ile Leu Phe Thr Ile
 145 150 155 160
 Pro Val Leu Val Leu Leu Ala Leu Gln Ser Asp Leu Gly Thr Ala Leu
 40 165 170 175
 Val Phe Val Ala Ile Phe Ser Gly Ile Val Leu Leu Ser Gly Val Ser
 180 185 190
 45 Trp Lys Ile Ile Ile Pro Val Phe Val Thr Ala Val Thr Gly Val Ala
 195 200 205
 Gly Phe Leu Ala Ile Phe Ile Ser Lys Asp Gly Arg Ala Phe Leu His
 210 215 220
 50 Gln Ile Gly Met Pro Thr Tyr Gln Ile Asn Arg Ile Leu Ala Trp Leu
 225 230 235 240
 Asn Pro Phe Glu Phe Ala Gln Thr Thr Thr Tyr Gln Gln Ala Gln Gly
 55 245 250 255
 Gln Ile Ala Ile Gly Ser Gly Gly Leu Phe Gly Gln Gly Phe Asn Ala

	260	265	270
5	Ser Asn Leu Leu Ile Pro Val Arg Glu Ser Asp Met Ile Phe Thr Val 275 280 285		
	Ile Ala Glu Asp Phe Gly Phe Ile Gly Ser Val Leu Val Ile Ala Leu 290 295 300		
10	Tyr Leu Met Leu Ile Tyr Arg Met Leu Lys Ile Thr Leu Lys Ser Asn 305 310 315 320		
	Asn Gln Phe Tyr Thr Tyr Ile Ser Thr Gly Leu Ile Met Met Leu Leu 325 330 335		
15	Phe His Ile Phe Glu Asn Ile Gly Ala Val Thr Gly Leu Leu Pro Leu 340 345 350		
	Thr Gly Ile Pro Leu Pro Phe Ile Ser Gln Gly Gly Ser Ala Ile Ile 355 360 365		
20	Ser Asn Leu Ile Gly Val Gly Leu Leu Leu Ser Met Ser Tyr Gln Thr 370 375 380		
25	Asn Leu Ala Glu Glu Lys Ser Gly Lys Val Pro Phe Lys Arg Lys Lys 385 390 395 400		
	Val Val Leu Lys Gln Ile Lys 405		
30	<210> 155 <211> 202 <212> PRT <213> Streptococcus pneumoniae		
35	<400> 155 Met Gly Lys Ile Ile Gly Ile Thr Gly Gly Ile Ala Ser Gly Lys Ser 1 5 10 15		
40	Thr Val Thr Asn Phe Leu Lys His Gln Gly Leu Ser Ser Ser Gly Leu 20 25 30		
	Pro Thr Gln Cys Ser Thr Asn Tyr Arg Lys Pro Gly Gly Arg Leu Phe 35 40 45		
45	Glu Ala Leu Val Gln His Phe Gly Gln Glu Ile Ile Leu Glu Asn Gly 50 55 60		
50	Glu Leu Asn Arg Pro Leu Ile Ala Ser Leu Ile Phe Ser Asn Pro Glu 65 70 75 80		
	Glu Gln Lys Trp Ser Asn Gln Ile Gln Gly Glu Ile Ile Arg Glu Glu 85 90 95		
55	Leu Ala Thr Leu Arg Glu Gln Leu Ala Gln Thr Glu Glu Ile Phe Phe 100 105 110		

Met Asp Ile Pro Leu Leu Phe Glu Gln Asp Tyr Ser Asp Trp Phe Ala
 115 120 125
 5 Glu Thr Trp Leu Val Tyr Val Asp Arg Asp Ala Gln Val Glu Arg Leu
 130 135 140
 Met Lys Arg Asp Gln Leu Ser Lys Asp Glu Ala Glu Ser Arg Met Ala
 145 150 155 160
 10 Ala Gln Trp Pro Leu Glu Lys Lys Lys Asp Leu Ala Ser Gln Val Leu
 165 170 175
 Asp Asn Asn Gly Asn Gln Asn Gln Leu Leu Asn Gln Val His Ile Leu
 180 185 190
 15 Leu Glu Gly Gly Arg Gln Asp Asp Arg Asp
 195 200
 20 <210> 156
 <211> 419
 <212> PRT
 <213> Streptococcus pneumoniae
 25 <400> 156
 Met Arg Lys Ile Val Ile Asn Gly Gly Leu Pro Leu Gln Gly Glu Ile
 1 5 10 15
 30 Thr Ile Ser Gly Ala Lys Asn Ser Val Val Ala Leu Ile Pro Ala Ile
 20 25 30
 Ile Leu Ala Asp Asp Val Val Thr Leu Asp Cys Val Pro Asp Ile Ser
 35 40 45
 35 Asp Val Ala Ser Leu Val Glu Ile Met Glu Leu Met Gly Ala Thr Val
 50 55 60
 Lys Arg Tyr Asp Asp Val Leu Glu Ile Asp Pro Arg Gly Val Gln Asn
 65 70 75 80
 40 Ile Pro Met Pro Tyr Gly Lys Ile Asn Ser Leu Arg Ala Ser Tyr Tyr
 85 90 95
 45 Phe Tyr Gly Ser Leu Leu Gly Arg Phe Gly Glu Ala Thr Val Gly Leu
 100 105 110
 Pro Gly Gly Cys Asp Leu Gly Pro Arg Pro Ile Asp Leu His Leu Lys
 115 120 125
 50 Ala Phe Glu Ala Met Gly Ala Thr Ala Ser Tyr Glu Gly Asp Asn Met
 130 135 140
 Lys Leu Ser Ala Lys Asp Thr Gly Leu His Gly Ala Ser Ile Tyr Met
 145 150 155 160
 55 Asp Thr Val Ser Val Gly Ala Thr Ile Asn Thr Met Ile Ala Ala Val
 165 170 175

Lys Ala Asn Gly Arg Thr Ile Ile Glu Asn Ala Ala Arg Glu Pro Glu
 180 185 190
 5 Ile Ile Asp Val Ala Thr Leu Leu Asn Asn Met Gly Ala His Ile Arg
 195 200 205
 Gly Ala Gly Thr Asn Ile Ile Ile Ile Asp Gly Val Glu Arg Leu His
 210 215 220
 10 Gly Thr Arg His Gln Val Ile Pro Asp Arg Ile Glu Ala Gly Thr Tyr
 225 230 235 240
 Ile Ser Leu Ala Ala Ala Val Gly Lys Gly Ile Arg Ile Asn Asn Val
 245 250 255
 Leu Tyr Glu His Leu Glu Gly Phe Ile Ala Lys Leu Glu Glu Met Gly
 260 265 270
 20 Val Arg Met Thr Val Ser Glu Asp Ser Ile Phe Val Glu Glu Gln Ser
 275 280 285
 Asn Leu Lys Ala Ile Asn Ile Lys Thr Ala Pro Tyr Pro Gly Phe Ala
 290 295 300
 25 Thr Asp Leu Gln Gln Pro Leu Thr Pro Leu Leu Leu Arg Ala Asn Gly
 305 310 315 320
 Arg Gly Thr Ile Val Asp Thr Ile Tyr Glu Lys Arg Val Asn His Val
 325 330 335
 Phe Glu Leu Ala Lys Met Asp Ala Asp Ile Ser Thr Thr Asn Gly His
 340 345 350
 35 Ile Leu Tyr Thr Gly Gly Arg Asp Leu Arg Gly Ala Ser Val Lys Ala
 355 360 365
 Thr Asp Leu Arg Ala Gly Ala Ala Leu Val Ile Ala Gly Leu Met Ala
 370 375 380
 40 Glu Gly Lys Thr Glu Ile Thr Asn Ile Glu Phe Ile Leu Arg Gly Tyr
 385 390 395 400
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	Val	His	Leu	Met	Val	Thr	Asp	Pro	Thr	Phe	Trp	Val	Asp	Gln	Val	Leu
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15	Asp	Leu	Gln	Cys	Glu	Tyr	Ile	Cys	Ile	His	Ala	Glu	Val	Leu	Asn	Gly
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	Leu	Ala	Phe	Arg	Leu	Ile	Asp	Lys	Ile	His	Asp	Ala	Gly	Leu	Lys	Ala
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	Ala	Gly	Gln	Arg	Phe	Leu	Glu	Ser	Thr	Leu	Tyr	Lys	Ile	Gln	Glu	Leu
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30	Arg	Gln	Leu	Arg	Val	Gln	Asn	Gly	Tyr	His	Tyr	Ile	Ile	Glu	Met	Asp
					165					170					175	
	Gly	Ser	Ser	Ser	Arg	Lys	Thr	Phe	Lys	Gln	Ile	Asp	Val	Ala	Gly	Pro
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			195					200					205			
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	Ala	Asn	Tyr	Pro	Phe	Ala	Thr	Ile	Asp	Pro	Asn	Val	Gly	Met	Val	Glu
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15	Glu	Asn	Val	Met	Arg	Glu	Gln	Gly	Arg	Glu	Asp	Ala	Phe	Val	Asp	Pro
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	Leu	Ala	Asp	Ile	Asp	Thr	Ile	Asn	Leu	Glu	Leu	Ile	Leu	Ala	Asp	Leu
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25	Gln	Lys	Asp	Lys	Glu	Ser	Val	Ala	Glu	Phe	Asn	Val	Leu	Gln	Lys	Ile
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	Lys	Pro	Val	Leu	Glu	Asp	Gly	Lys	Ser	Ala	Arg	Thr	Ile	Glu	Phe	Thr
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			195					200					205			
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	Asp	Ser	Ile	Asp	Tyr	Val	Lys	Gln	Ile	Arg	Glu	Phe	Ala	Ala	Thr	Glu
	225					230					235					240
40	Asn	Ala	Glu	Val	Val	Val	Ile	Ser	Ala	Arg	Ala	Glu	Glu	Glu	Ile	Ser
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	Glu	Leu	Asp	Asp	Glu	Asp	Lys	Lys	Glu	Phe	Leu	Glu	Ala	Ile	Gly	Leu
			260						265					270		
45	Thr	Glu	Ser	Gly	Val	Asp	Lys	Leu	Thr	Arg	Ala	Ala	Tyr	His	Leu	Leu
			275					280					285			
	Gly	Leu	Gly	Thr	Tyr	Phe	Thr	Ala	Gly	Glu	Lys	Glu	Val	Arg	Ala	Trp
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	Thr	Phe	Lys	Arg	Gly	Met	Lys	Ala	Pro	Gln	Ala	Ala	Gly	Ile	Ile	His
	305					310					315					320
55	Ser	Asp	Phe	Glu	Lys	Gly	Phe	Ile	Arg	Ala	Val	Thr	Met	Ser	Tyr	Glu
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 Ala Asp Asp Tyr Ser Leu Ala Glu Ile Ala Glu Glu Phe Gly Val Ser
 35 40 45
 25 Arg Gln Ala Val Tyr Asp Asn Ile Lys Arg Thr Glu Lys Ile Leu Glu
 50 55 60
 30 Asp Tyr Glu Met Lys Leu His Met Tyr Ser Asp Tyr Ile Val Arg Ser
 65 70 75 80
 Gln Ile Phe Asp Gln Ile Leu Glu Arg Tyr Pro Lys Asp Asp Phe Leu
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 35 40 45
 55 Ile Glu Ser Ile Lys Glu Lys Met Ala Arg Arg Gly Ile Thr Tyr Ala
 50 55 60
 Thr Leu Glu His Asp Leu Gln Asp Ile Ala Gly Leu Arg Val Met Val

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	Gln	Asp	Met	Arg	Ile	Ile	Gln	Glu	Arg	Asp	Tyr	Ile	Thr	His	Arg	Lys
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10	Ala	Ser	Gly	Tyr	Arg	Ser	Tyr	His	Val	Val	Val	Glu	Tyr	Thr	Val	Asp
			115					120					125			
	Thr	Ile	Asn	Gly	Ala	Lys	Thr	Ile	Leu	Ala	Glu	Ile	Gln	Ile	Arg	Thr
		130					135					140				
15	Leu	Ala	Met	Asn	Phe	Trp	Ala	Thr	Ile	Glu	His	Ser	Leu	Asn	Tyr	Lys
	145					150					155					160
	Tyr	Gln	Gly	Asp	Phe	Pro	Asp	Glu	Ile	Lys	Lys	Arg	Leu	Glu	Ile	Thr
					165					170					175	
20	Ala	Arg	Ile	Ala	His	Gln	Leu	Asp	Glu	Glu	Met	Gly	Glu	Ile	Arg	Asp
				180					185					190		
25	Asp	Ile	Gln	Glu	Ala	Gln	Ala	Leu	Phe	Asp	Pro	Leu	Ser	Arg	Lys	Leu
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	Arg	Ser	Asn	Val	Gly	Lys	Ser	Ser	Phe	Ile	Asn	Thr	Met	Leu	Asn	Arg
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		50					55					60				
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	Tyr	Gly	Tyr	Ala	Arg	Val	Ser	Lys	Lys	Glu	Arg	Glu	Lys	Trp	Gly	Cys
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55	Met	Ile	Glu	Glu	Tyr	Leu	Thr	Thr	Arg	Glu	Asn	Leu	Arg	Ala	Val	Val
				100					105					110		

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 5 Tyr Glu Phe Leu Lys Tyr Tyr Glu Ile Pro Val Ile Ile Val Ala Thr
 130 135 140
 Lys Ala Asp Lys Ile Pro Arg Gly Lys Trp Asn Lys His Glu Ser Ala
 145 150 155 160
 10 Ile Lys Lys Lys Leu Asn Phe Asp Pro Ser Asp Asp Phe Ile Leu Phe
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 Ser Ser Val Ser Lys Ala Gly Met Asp Glu Ala Trp Asp Ala Ile Leu
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 15 Glu Lys Leu
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 20 25 30
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 35 35 40 45
 35 Ile Lys Leu Asp Asn Ala Glu Ala Leu Glu Ala Lys Lys Lys Lys Val
 50 55 60
 Phe Asn Arg Ser Phe Ser Met Glu Val Glu Glu Ser Phe Tyr Asp Glu
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	Arg	Lys	Glu	Glu	Glu	Glu	Lys	Lys	Ile	Lys	Glu	Gln	Ile	Ala	Lys	Glu	
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	Thr	Leu	Lys	Pro	Ile	Ile	Gln	Ile	Gly	Lys	Asn	Gly	Leu	Asn	Asp	Gln	
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30	Ile	Lys	Thr	Ser	Val	Arg	Gln	Ala	Leu	Asp	Ala	Arg	Glu	Leu	Ile	Lys	
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	Val	Thr	Leu	Leu	Gln	Asn	Thr	Asp	Glu	Asn	Ile	His	Glu	Val	Ala	Glu	
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	Ile	Leu	Glu	Glu	Glu	Ile	Gly	Val	Asp	Thr	Val	Gln	Lys	Ile	Gly	Arg	
		65				70					75					80	
40	Ile	Leu	Ile	Leu	Phe	Lys	Gln	Ser	Ser	Lys	Lys	Glu	Asn	Arg	Lys	Ile	
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 5 Pro Glu Met Lys Gln Trp Leu His Asp Leu Arg Asp Ala Gly Ile Gly
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 Ile Ile Val Val Ser Asn Asn Thr Lys Lys Arg Val Gln Arg Ala Val
 65 70 75 80
 10 Glu Lys Phe Gly Ile Asp Tyr Val Tyr Trp Ala Leu Lys Pro Phe Thr
 85 90 95
 15 Phe Gly Ile Asp Arg Ala Met Lys Glu Phe His Tyr Asp Lys Lys Glu
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 Val Val Met Val Gly Asp Gln Leu Met Thr Asp Ile Arg Ala Ala His
 115 120 125
 20 Arg Ala Gly Ile Arg Ser Ile Leu Val Lys Pro Leu Val Gln His Asp
 130 135 140
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 Ser Thr Ala Asp Lys Glu Ala Leu His Thr Leu Leu Ala Asp Glu Ala
 35 40 45
 45 Val Cys Ile Gly Pro Gly Lys Ala Thr Glu Ser Tyr Leu Asn Ile Asn
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 Ala Val Leu Ser Ala Ala Val Leu Thr Glu Ala Glu Ala Ile His Pro
 65 70 75 80
 50 Gly Phe Gly Phe Leu Ser Glu Asn Ser Lys Phe Ala Thr Met Cys Glu
 85 90 95
 55 Glu Ile Gly Ile Lys Phe Ile Gly Pro Ser Gly His Val Met Asp Met
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 Met Gly Asp Lys Ile Asn Ala Arg Ala Gln Met Ile Lys Ala Gly Val

	115	120	125	
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10	Ala Gly Gly Gly Gly Lys Gly Ile Arg Lys Val Glu Lys Pro Asp Asp 165 170 175			
	Leu Val Ser Ala Phe Glu Thr Ala Ser Ser Glu Ala Lys Ala Asn Tyr 180 185 190			
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20	Ile Glu Val Gln Ile Leu Gly Asp Glu His Gly His Val Ile His Leu 210 215 220			
	Gly Glu Arg Asp Cys Ser Leu Gln Arg Asn Asn Gln Lys Val Leu Glu 225 230 235 240			
25	Glu Ser Pro Ser Ile Ala Ile Gly Lys Thr Leu Arg His Glu Ile Gly 245 250 255			
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	Glu Cys Arg Ile Asn Ala Glu Asn Pro Ala Phe Asn Phe Ala Pro Ser 340 345 350			
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50	Arg Val Asp Ser Ala Val Tyr Pro Gly Tyr Thr Ile Pro Pro Tyr Tyr 370 375 380			
	Asp Ser Met Ile Ala Lys Ile Ile Val His Gly Glu Asn Arg Phe Asp 385 390 395 400			
55	Ala Leu Met Lys Met Gln Arg Ala Leu Tyr Glu Leu Glu Ile Glu Gly 405 410 415			
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 Val Ile Ala Gly Asp Tyr Asp Thr Cys Phe Leu Met Glu Thr Phe Leu
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 35 40 45
 Val Ala Ser Arg His His Val Glu Val Ile Thr Ala Cys Ile Glu Glu
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 Val Thr Tyr Gly Pro Gly Leu Val Gly Ala Leu Leu Val Gly Leu Ser
 85 90 95
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Asn His Met Ala Gly His Leu Met Ala Ala Gln Ser Val Glu Pro Leu
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 5 Glu Phe Pro Leu Leu Ala Leu Leu Val Ser Gly Gly His Thr Glu Leu
 130 135 140
 Val Tyr Val Ser Glu Ala Gly Asp Tyr Lys Ile Val Gly Glu Thr Arg
 145 150 155 160
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 15 Leu Thr Tyr Pro Ala Gly Arg Glu Ile Asp Glu Leu Ala His Gln Gly
 180 185 190
 Gln Asp Ile Tyr Asp Phe Pro Arg Ala Met Ile Lys Glu Asp Asn Leu
 195 200 205
 20 Glu Phe Ser Phe Ser Gly Leu Lys Ser Ala Phe Ile Asn Leu His His
 210 215 220
 Asn Ala Glu Gln Lys Gly Glu Ser Leu Ser Thr Glu Asp Leu Cys Ala
 225 230 235 240
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 260 265 270
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	Ile	Asp	Ser	Glu	Asn	Pro	Asp	Val	Ile	Tyr	Val	Ala	Lys	Asn	Lys	Ser
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	Thr	Val	Thr	Asn	Val	Pro	Gly	Ser	Thr	Leu	Ser	Arg	Glu	Ala	Asn	Tyr
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	Thr	Met	Leu	Leu	His	Ala	Gly	Pro	Glu	Ile	Ala	Val	Ala	Ser	Thr	Lys
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15	Ala	Tyr	Thr	Ala	Gln	Ile	Ala	Ala	Leu	Ala	Phe	Leu	Ala	Lys	Ala	Val
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	Gly	Glu	Ala	Asn	Gly	Asn	Ala	Lys	Ala	Gln	Ala	Phe	Asp	Leu	Val	His
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	Glu	Leu	Ser	Ile	Val	Ala	Gln	Ser	Ile	Glu	Ser	Thr	Leu	Ser	Glu	Lys
			435					440					445			
25	Glu	Thr	Ile	Glu	Ala	Lys	Val	Arg	Glu	Leu	Leu	Glu	Thr	Thr	Arg	Asn
	450						455					460				
	Ala	Phe	Tyr	Ile	Gly	Arg	Gly	Gln	Asp	Tyr	Tyr	Val	Ala	Met	Glu	Ala
	465					470				475						480
30	Ser	Leu	Lys	Leu	Lys	Glu	Ile	Ser	Tyr	Ile	Gln	Cys	Glu	Gly	Phe	Ala
					485					490					495	
	Ala	Gly	Glu	Leu	Lys	His	Gly	Thr	Ile	Ala	Leu	Ile	Glu	Glu	Gly	Thr
35				500					505					510		
	Pro	Val	Leu	Ala	Leu	Leu	Ser	Asp	Pro	Val	Leu	Ala	Asn	His	Thr	Arg
			515					520					525			
40	Gly	Asn	Ile	Gln	Glu	Val	Ala	Ala	Arg	Gly	Ala	Lys	Val	Leu	Thr	Ile
	530						535					540				
	Ala	Glu	Glu	Asn	Val	Ala	Lys	Asp	Thr	Asp	Asp	Ile	Val	Leu	Thr	Thr
	545					550				555						560
45	Val	His	Pro	Tyr	Leu	Ser	Pro	Ile	Ser	Met	Val	Val	Pro	Thr	Gln	Leu
					565					570					575	
	Val	Ala	Tyr	Phe	Ala	Thr	Leu	His	Arg	Gly	Leu	Asp	Val	Asp	Lys	Pro
				580					585					590		
50	Arg	Asn	Leu	Ala	Lys	Ser	Val	Thr	Val	Glu						
			595					600								
55	<210>	170														
	<211>	240														
	<212>	PRT														

<213> Streptococcus pneumoniae

<400> 170

5 Met Ile Arg Ile Glu Asn Leu Ser Val Ser Tyr Lys Glu Thr Leu Ala
 1 5 10 15
 Leu Lys Asp Ile Ser Leu Val Leu His Gly Pro Thr Ile Thr Gly Ile
 20 25 30
 10 Ile Gly Pro Asn Gly Ala Gly Lys Ser Thr Leu Leu Lys Gly Met Leu
 35 40 45
 Gly Ile Ile Pro His Gln Gly Gln Ala Phe Leu Asp Asp Lys Glu Val
 50 55 60
 15 Lys Lys Ser Leu His Arg Ile Ala Tyr Val Glu Gln Lys Ile Asn Ile
 65 70 75 80
 20 Asp Tyr Asn Phe Pro Ile Lys Val Lys Glu Cys Val Ser Leu Gly Leu
 85 90 95
 Phe Pro Ser Ile Pro Leu Phe Arg Ser Leu Lys Ala Lys His Trp Lys
 100 105 110
 25 Lys Val Gln Glu Ala Leu Glu Ile Val Gly Leu Ala Asp Tyr Ala Glu
 115 120 125
 Arg Gln Ile Ser Gln Leu Ser Gly Gly Gln Phe Gln Arg Val Leu Ile
 130 135 140
 30 Ala Arg Cys Leu Val Gln Glu Ala Asp Tyr Ile Leu Leu Asp Glu Pro
 145 150 155 160
 Phe Ala Gly Ile Asp Ser Val Ser Glu Glu Ile Ile Met Asn Thr Leu
 165 170 175
 35 Arg Asp Leu Lys Lys Ala Gly Lys Thr Val Leu Ile Val His His Asp
 180 185 190
 40 Leu Ser Lys Ile Pro His Tyr Phe Asp Gln Val Leu Leu Val Asn Arg
 195 200 205
 Glu Val Ile Ala Phe Gly Pro Thr Lys Glu Thr Phe Thr Glu Thr Asn
 210 215 220
 45 Leu Lys Glu Ala Tyr Gly Asn Gln Leu Phe Phe Asn Gly Gly Asp Leu
 225 230 235 240

50

<210> 171

<211> 740

55 <212> PRT

<213> Streptococcus pneumoniae

<400> 171
 Met Pro Lys Glu Val Asn Leu Thr Gly Glu Glu Val Val Ala Leu Thr
 1 5 10 15
 5 Lys Glu Tyr Leu Thr Glu Glu Asp Val His Phe Val His Lys Ala Leu
 20 25 30
 Val Tyr Ala Val Glu Cys His Ser Gly Gln Tyr Arg Lys Ser Gly Glu
 35 40 45
 10 Pro Tyr Ile Ile His Pro Ile Gln Val Ala Gly Ile Leu Ala Lys Leu
 50 55 60
 15 Lys Leu Asp Ala Val Thr Val Ala Cys Gly Phe Leu His Asp Val Val
 65 70 75 80
 Glu Asp Thr Asp Ala Thr Leu Asp Asp Leu Glu Arg Glu Phe Gly Pro
 85 90 95
 20 Asp Val Arg Val Ile Val Asp Gly Val Thr Lys Leu Gly Lys Val Glu
 100 105 110
 Tyr Lys Ser Ile Glu Glu Gln Leu Ala Glu Asn His Arg Lys Met Leu
 115 120 125
 25 Met Ala Met Ser Glu Asp Ile Arg Val Ile Leu Val Lys Leu Ser Asp
 130 135 140
 Arg Leu His Asn Met Arg Thr Leu Lys His Leu Arg Lys Asp Lys Gln
 145 150 155 160
 Glu Arg Ile Ser Lys Glu Thr Met Glu Ile Tyr Ala Pro Leu Ala His
 165 170 175
 35 Arg Leu Gly Ile Ser Ser Val Lys Trp Glu Leu Glu Asp Leu Ser Phe
 180 185 190
 Arg Tyr Leu Asn Pro Thr Glu Phe Tyr Lys Ile Thr His Met Met Lys
 195 200 205
 40 Glu Lys Arg Arg Glu Arg Glu Ala Leu Val Asp Glu Val Val Thr Lys
 210 215 220
 Leu Glu Glu Tyr Thr Thr Glu Arg His Leu Lys Gly Lys Ile Tyr Gly
 225 230 235 240
 Arg Pro Lys His Ile Tyr Ser Ile Phe Arg Lys Met Gln Asp Lys Arg
 245 250 255
 50 Lys Arg Phe Glu Glu Ile Tyr Asp Leu Ile Ala Ile Arg Cys Ile Leu
 260 265 270
 Asp Thr Gln Ser Asp Val Tyr Ala Met Leu Gly Tyr Val His Glu Phe
 275 280 285
 55 Trp Lys Pro Met Pro Gly Arg Phe Lys Asp Tyr Ile Ala Asn Arg Lys
 290 295 300

	Ala	Asn	Gly	Tyr	Gln	Ser	Ile	His	Thr	Thr	Val	Tyr	Gly	Pro	Lys	Gly	
	305					310					315					320	
5	Pro	Ile	Glu	Phe	Gln	Ile	Arg	Thr	Lys	Glu	Met	His	Glu	Val	Ala	Glu	
					325					330					335		
	Tyr	Gly	Val	Ala	Ala	His	Trp	Ala	Tyr	Lys	Lys	Gly	Ile	Lys	Gly	Gln	
				340					345					350			
10	Val	Asn	Ser	Lys	Glu	Ser	Ala	Ile	Gly	Met	Asn	Trp	Ile	Lys	Glu	Met	
			355					360					365				
	Met	Glu	Leu	Gln	Asp	Gln	Ala	Asp	Asp	Ala	Lys	Glu	Phe	Val	Asp	Ser	
15		370					375					380					
	Val	Lys	Glu	Asn	Tyr	Leu	Ala	Glu	Glu	Ile	Tyr	Val	Phe	Thr	Pro	Asp	
	385					390					395					400	
20	Gly	Ala	Val	Arg	Ser	Leu	Pro	Lys	Asp	Ser	Gly	Pro	Ile	Asp	Phe	Ala	
					405					410					415		
	Tyr	Glu	Ile	His	Thr	Lys	Val	Gly	Glu	Lys	Ala	Thr	Gly	Ala	Lys	Val	
				420					425					430			
25	Asn	Gly	Arg	Met	Val	Pro	Leu	Thr	Thr	Lys	Leu	Lys	Thr	Gly	Asp	Gln	
			435					440					445				
	Val	Glu	Ile	Ile	Ala	Asn	Pro	Asn	Ser	Phe	Gly	Pro	Ser	Arg	Asp	Trp	
30		450					455					460					
	Leu	Asn	Met	Val	Lys	Thr	Ser	Lys	Ala	Arg	Asn	Lys	Ile	Arg	Gln	Phe	
	465					470					475					480	
35	Phe	Lys	Asn	Gln	Asp	Lys	Glu	Leu	Ser	Val	Asn	Lys	Gly	Arg	Glu	Met	
					485					490					495		
	Leu	Met	Ala	Gln	Phe	Gln	Glu	Asn	Gly	Tyr	Val	Ala	Asn	Lys	Phe	Met	
				500					505					510			
40	Asp	Lys	Arg	His	Met	Asp	Gln	Val	Leu	Gln	Lys	Thr	Ser	Tyr	Lys	Thr	
			515					520					525				
	Glu	Asp	Ser	Leu	Phe	Ala	Ala	Ile	Gly	Phe	Gly	Glu	Ile	Gly	Ala	Ile	
45		530					535					540					
	Thr	Val	Phe	Asn	Arg	Leu	Thr	Glu	Lys	Glu	Arg	Arg	Glu	Glu	Glu	Arg	
	545					550					555					560	
50	Ala	Lys	Ala	Lys	Ala	Glu	Ala	Glu	Glu	Leu	Val	Lys	Gly	Gly	Glu	Val	
					565					570					575		
	Lys	Val	Glu	Asn	Lys	Glu	Thr	Leu	Lys	Val	Lys	His	Glu	Gly	Gly	Val	
				580					585					590			
55	Val	Ile	Glu	Gly	Ala	Ser	Gly	Leu	Leu	Val	Arg	Ile	Ala	Lys	Cys	Cys	
			595					600					605				

Asn Pro Val Pro Gly Asp Asp Ile Val Gly Tyr Ile Thr Lys Gly Arg
 610 615 620
 5 Gly Val Ala Ile His Arg Val Asp Cys Met Asn Leu Arg Ala Gln Glu
 625 630 635 640
 Asn Tyr Glu Gln Arg Leu Leu Asp Val Glu Trp Glu Asp Gln Tyr Ser
 645 650 655
 10 Ser Ser Asn Lys Glu Tyr Leu Ala His Ile Asp Ile Tyr Gly Leu Asn
 660 665 670
 Arg Thr Gly Leu Leu Asn Asp Val Leu Gln Val Leu Ser Asn Thr Thr
 675 680 685
 15 Lys Asn Ile Ser Thr Val Asn Ala Gln Pro Thr Lys Asp Met Lys Phe
 690 695 700
 20 Ala Asn Ile His Val Ser Phe Gly Ile Ala Asn Leu Ser Thr Leu Thr
 705 710 715 720
 Thr Val Val Asp Lys Ile Lys Ser Val Pro Glu Val Tyr Ser Val Lys
 725 730 735
 25 Arg Thr Asn Gly
 740
 30 <210> 172
 <211> 492
 <212> PRT
 <213> Streptococcus pneumoniae
 35 <400> 172
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 40 Asp Val Leu Leu Ile Pro Ala Glu Ser His Val Leu Pro Asn Asp Ala
 20 25 30
 Asp Leu Thr Thr Lys Leu Ala Asp Asn Leu Thr Leu Asn Ile Pro Ile
 35 40 45
 45 Ile Thr Ala Ala Met Asp Thr Val Thr Glu Ser Gln Met Ala Ile Ala
 50 55 60
 Ile Ala Arg Ala Gly Gly Leu Gly Val Ile His Lys Asn Met Ser Ile
 65 70 75 80
 50 Ala Gln Gln Ala Asp Glu Val Arg Lys Val Lys Arg Ser Glu Asn Gly
 85 90 95
 55 Val Ile Ile Asp Pro Phe Phe Leu Thr Pro Glu His Thr Ile Ala Glu
 100 105 110
 Ala Asp Glu Leu Met Gly Arg Tyr Arg Ile Ser Gly Val Pro Val Val

	115	120	125
	Glu Thr Leu Glu Asn Arg Lys Leu Val Gly Ile Leu Thr Asn Arg Asp		
	130	135	140
5	Leu Arg Phe Ile Ser Asp Tyr Asn Gln Pro Ile Ser Asn His Met Thr		
	145	150	155
	Ser Glu Asn Leu Val Thr Ala Pro Val Gly Thr Asp Leu Ala Thr Ala		
10		165	170
	Glu Ser Ile Leu Gln Glu His Arg Ile Glu Lys Leu Pro Leu Val Asp		
	180	185	190
15	Glu Glu Gly Ser Leu Ser Gly Leu Ile Thr Ile Lys Asp Ile Glu Lys		
	195	200	205
	Val Ile Glu Phe Pro Asn Ala Ala Lys Asp Glu Phe Gly Arg Leu Leu		
20		210	215
	Val Ala Gly Ala Val Gly Val Thr Ser Asp Thr Phe Glu Arg Ala Glu		
	225	230	235
	Ala Leu Phe Glu Ala Gly Ala Asp Ala Ile Val Ile Asp Thr Ala His		
25		245	250
	Gly His Ser Ala Gly Val Leu Arg Lys Ile Ala Glu Ile Arg Ala His		
	260	265	270
30	Phe Pro Asp Arg Thr Leu Ile Ala Gly Asn Ile Ala Thr Ala Glu Gly		
	275	280	285
	Ala Arg Ala Leu Tyr Glu Ala Gly Val Asp Val Val Lys Val Gly Ile		
35		295	300
	Gly Pro Gly Ser Ile Cys Thr Thr Arg Val Ile Ala Gly Val Gly Val		
	305	310	315
	Pro Gln Val Thr Ala Ile Tyr Asp Ala Ala Ala Val Ala Arg Glu Tyr		
40		325	330
	Gly Lys Thr Ile Ile Ala Asp Gly Gly Ile Lys Tyr Ser Gly Asp Ile		
	340	345	350
45	Val Lys Ala Leu Ala Ala Gly Gly Asn Ala Val Met Leu Gly Ser Met		
	355	360	365
	Phe Ala Gly Thr Asp Glu Ala Pro Gly Glu Thr Glu Ile Phe Gln Gly		
50		375	380
	Arg Lys Phe Lys Thr Tyr Arg Gly Met Gly Ser Ile Ala Ala Met Lys		
	385	390	395
55	Lys Gly Ser Ser Asp Arg Tyr Phe Gln Gly Ser Val Asn Glu Ala Asn		
	405	410	415
	Lys Leu Val Pro Glu Gly Ile Glu Gly Arg Val Ala Tyr Lys Gly Ala		

[illegible]

	Lys	Leu	Asn	Lys	Arg	Ile	Gln	Glu	Leu	Ala	Phe	Leu	Asn	Arg	Gly	Leu	
			195					200					205				
5	Gln	Ile	Ser	Ile	Thr	Asp	Lys	Arg	Gln	Gly	Leu	Glu	Gln	Thr	Lys	His	
		210					215					220					
	Tyr	His	Tyr	Glu	Gly	Gly	Ile	Ala	Ser	Tyr	Val	Glu	Tyr	Ile	Asn	Glu	
	225					230					235					240	
10	Asn	Lys	Asp	Val	Ile	Phe	Asp	Thr	Pro	Ile	Tyr	Thr	Asp	Gly	Glu	Met	
					245					250					255		
	Asp	Asp	Ile	Thr	Val	Glu	Val	Ala	Met	Gln	Tyr	Thr	Thr	Gly	Tyr	His	
15				260					265					270			
	Glu	Asn	Val	Met	Ser	Phe	Ala	Asn	Asn	Ile	His	Thr	His	Glu	Gly	Gly	
			275					280					285				
20	Thr	His	Glu	Gln	Gly	Phe	Arg	Thr	Ala	Leu	Thr	Arg	Val	Ile	Asn	Asp	
		290					295					300					
	Tyr	Ala	Arg	Lys	Asn	Lys	Leu	Leu	Lys	Asp	Asn	Glu	Asp	Asn	Leu	Thr	
	305					310				315						320	
25	Gly	Glu	Asp	Val	Arg	Glu	Gly	Leu	Thr	Ala	Val	Ile	Ser	Val	Lys	His	
					325					330					335		
	Pro	Asn	Pro	Gln	Phe	Glu	Gly	Gln	Thr	Lys	Thr	Lys	Leu	Gly	Asn	Ser	
30				340					345					350			
	Glu	Val	Val	Lys	Ile	Thr	Asn	Arg	Leu	Phe	Ser	Glu	Ala	Phe	Ser	Asp	
			355					360					365				
35	Phe	Leu	Met	Glu	Asn	Pro	Gln	Ile	Ala	Lys	Arg	Ile	Val	Glu	Lys	Gly	
	370						375					380					
	Ile	Leu	Ala	Ala	Lys	Ala	Arg	Val	Ala	Ala	Lys	Arg	Ala	Arg	Glu	Val	
	385					390					395					400	
40	Thr	Arg	Lys	Lys	Ser	Gly	Leu	Glu	Ile	Ser	Asn	Leu	Pro	Gly	Lys	Leu	
					405					410					415		
	Ala	Asp	Cys	Ser	Ser	Asn	Asn	Pro	Ala	Glu	Thr	Glu	Leu	Phe	Ile	Val	
45				420				425						430			
	Glu	Gly	Asp	Ser	Ala	Gly	Gly	Ser	Ala	Lys	Ser	Gly	Arg	Asn	Arg	Glu	
			435					440					445				
50	Phe	Gln	Ala	Ile	Leu	Pro	Ile	Arg	Gly	Lys	Ile	Leu	Asn	Val	Glu	Lys	
	450						455					460					
	Ala	Ser	Met	Asp	Lys	Ile	Leu	Ala	Asn	Glu	Glu	Ile	Arg	Ser	Leu	Phe	
	465					470					475					480	
55	Thr	Ala	Met	Gly	Thr	Gly	Phe	Gly	Ala	Glu	Phe	Asp	Val	Ser	Lys	Ala	
					485					490					495		

Arg Tyr Gln Lys Leu Val Leu Met Thr Asp Ala Asp Val Asp Gly Ala
 500 505 510

5 His Ile Arg Thr Leu Leu Leu Thr Leu Ile Tyr Arg Tyr Met Lys Pro
 515 520 525

Ile Leu Glu Ala Gly Tyr Val Tyr Ile Ala Gln Pro Pro Ile Tyr Gly
 530 535 540

10 Val Lys Val Gly Ser Glu Ile Lys Glu Tyr Ile Gln Pro Gly Ala Asp
 545 550 555 560

Gln Glu Ile Lys Leu Gln Glu Ala Leu Ala Arg Tyr Ser Glu Gly Arg
 565 570 575

15 Thr Lys Pro Thr Ile Gln Arg Tyr Lys Gly Leu Gly Glu Met Asp Asp
 580 585 590

20 His Gln Leu Trp Glu Thr Thr Met Asp Pro Glu His Arg Leu Met Ala
 595 600 605

Arg Val Ser Val Asp Asp Ala Ala Glu Ala Asp Lys Ile Phe Asp Met
 610 615 620

25 Leu Met Gly Asp Arg Val Glu Pro Arg Arg Glu Phe Ile Glu Glu Asn
 625 630 635 640

Ala Val Tyr Ser Thr Leu Asp Val
 645

30

<210> 174
 <211> 88
 <212> PRT
 35 <213> Streptococcus pneumoniae

<400> 174
 Met Gly Phe Thr Glu Glu Thr Val Arg Phe Lys Leu Asp Asp Ser Asn
 1 5 10 15

40 Lys Lys Glu Ile Ser Glu Thr Leu Thr Asp Val Tyr Ala Ser Leu Asn
 20 25 30

45 Asp Lys Gly Tyr Asn Pro Ile Asn Gln Ile Val Gly Tyr Val Leu Ser
 35 40 45

Gly Asp Pro Ala Tyr Val Pro Arg Tyr Asn Asn Ala Arg Asn Gln Ile
 50 55 60

50 Arg Lys Tyr Glu Arg Asp Glu Ile Val Glu Glu Leu Val Arg Tyr Tyr
 65 70 75 80

Leu Lys Gly Gln Gly Val Asp Leu
 85

55

<210> 175

<211> 198

<212> PRT

<213> Streptococcus pneumoniae

5 <400> 175

Met Val Asn Tyr Pro His Lys Val Ser Ser Gln Asp Arg Gln Thr Ser
 1 5 10 15

10

Leu Ser Gln Pro Lys Asn Phe Ala Asn Arg Gly Met Ser Phe Glu Lys
 20 25 30

Met Ile Asn Ala Thr Asn Asp Tyr Tyr Leu Ser Gln Gly Leu Ala Val
 35 40 45

15

Ile His Lys Lys Pro Thr Pro Ile Gln Ile Val Gln Val Asp Tyr Pro
 50 55 60

Gln Arg Ser Arg Ala Lys Ile Val Glu Ala Tyr Phe Arg Gln Ala Ser
 65 70 75 80

20

Thr Thr Asp Tyr Ser Gly Val Tyr Asn Gly Tyr Tyr Ile Asp Phe Glu
 85 90 95

25

Val Lys Glu Thr Lys Gln Lys Arg Ala Ile Pro Met Lys Asn Phe His
 100 105 110

Pro His Gln Ile Gln His Met Glu Gln Val Leu Ala Gln Gln Gly Ile
 115 120 125

30

Cys Phe Val Leu Leu His Phe Ser Ser Gln Gln Glu Thr Tyr Leu Leu
 130 135 140

Pro Ala Phe Asp Leu Ile Arg Phe Tyr His Gln Asp Lys Gly Gln Lys
 145 150 155 160

35

Ser Met Pro Leu Glu Tyr Ile Arg Glu Tyr Gly Tyr Glu Ile Lys Ala
 165 170 175

40

Gly Ala Phe Pro Gln Ile Pro Tyr Leu Asn Val Ile Lys Glu His Leu
 180 185 190

Leu Gly Gly Lys Thr Arg
 195

45

<210> 176

<211> 288

<212> PRT

<213> Streptococcus pneumoniae

50

<400> 176

Met Ala Leu Phe Ser Lys Lys Asp Lys Tyr Ile Arg Ile Asn Pro Asn
 1 5 10 15

55

Arg Ser Val Arg Glu Lys Pro Gln Ala Lys Pro Glu Val Pro Asp Glu
 20 25 30

Leu Phe Ser Gln Cys Pro Gly Cys Lys His Thr Ile Tyr Gln Lys Asp
 35 40 45
 5 Leu Gly Ser Glu Arg Ile Cys Pro His Cys Ser Tyr Thr Phe Arg Ile
 50 55 60
 Ser Ala Gln Glu Arg Leu Ala Leu Thr Ile Asp Met Gly Thr Phe Lys
 65 70 75 80
 10 Glu Leu Phe Thr Gly Ile Glu Ser Lys Asp Pro Leu His Phe Pro Gly
 85 90 95
 Tyr Gln Lys Lys Leu Ala Ser Met Arg Glu Lys Thr Gly Leu His Glu
 100 105 110
 15 Ala Val Val Thr Gly Thr Ala Leu Ile Lys Gly Gln Thr Val Ala Leu
 115 120 125
 20 Gly Ile Met Asp Ser Asn Phe Ile Met Ala Ser Met Gly Thr Val Val
 130 135 140
 Gly Glu Lys Ile Thr Arg Leu Phe Glu Tyr Ala Thr Val Glu Lys Leu
 145 150 155 160
 25 Pro Val Val Leu Phe Thr Ala Ser Gly Gly Ala Arg Met Gln Glu Gly
 165 170 175
 Ile Met Ser Leu Met Gln Met Ala Lys Ile Ser Ala Ala Val Lys Arg
 180 185 190
 30 His Ser Asn Ala Gly Leu Phe Tyr Leu Thr Ile Leu Thr Asp Pro Thr
 195 200 205
 35 Thr Gly Gly Val Thr Ala Ser Phe Ala Met Glu Gly Asp Ile Ile Leu
 210 215 220
 Ala Glu Pro Gln Ser Leu Val Gly Phe Ala Gly Arg Arg Val Ile Glu
 225 230 235 240
 40 Asn Thr Val Arg Glu Ser Leu Pro Glu Asp Phe Gln Lys Ala Glu Phe
 245 250 255
 Leu Leu Glu His Gly Phe Val Asp Ala Ile Val Lys Arg Arg Asp Leu
 260 265 270
 45 Pro Asp Thr Ile Ala Ser Leu Val Arg Leu His Gly Gly Ser Pro Arg
 275 280 285
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 55 <210> 177
 <211> 139
 <212> PRT
 <213> Streptococcus pneumoniae

<400> 177
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 5 Ile Ser Asp Pro Leu Gly Phe Thr Ala Gln Gly Leu Glu Ile Ile Gln
 20 25 30
 Ile Asn Glu Glu Gln Gly Gln Phe Gly Ser Asp Arg Val Lys Glu Leu
 35 40 45
 10 Val Asp Thr Tyr Lys Val Glu Arg Phe Val Val Gly Leu Pro Lys Asn
 50 55 60
 15 Met Asn Asn Thr Ser Gly Pro Arg Val Glu Ala Ser Gln Ala Tyr Gly
 65 70 75 80
 Ala Lys Leu Glu Glu Phe Phe Gly Leu Pro Val Asp Tyr Gln Asp Glu
 85 90 95
 20 Arg Leu Thr Thr Val Ala Ala Glu Arg Met Leu Ile Glu Gln Ala Asp
 100 105 110
 Ile Ser Arg Asn Lys Arg Lys Lys Val Ile Asp Lys Leu Ala Ala Gln
 115 120 125
 25 Leu Ile Leu Gln Asn Tyr Leu Asp Arg Lys Phe
 130 135
 30 <210> 178
 <211> 398
 <212> PRT
 <213> Streptococcus pneumoniae
 35 <400> 178
 Met Ala Lys Leu Thr Val Lys Asp Val Asp Leu Lys Gly Lys Lys Val
 1 5 10 15
 40 Leu Val Arg Val Asp Phe Asn Val Pro Leu Lys Asp Gly Val Ile Thr
 20 25 30
 Asn Asp Asn Arg Ile Thr Ala Ala Leu Pro Thr Ile Lys Tyr Ile Ile
 35 40 45
 45 Glu Gln Gly Gly Arg Ala Ile Leu Phe Ser His Leu Gly Arg Val Lys
 50 55 60
 Glu Glu Ala Asp Lys Ala Gly Lys Ser Leu Ala Pro Val Ala Ala Asp
 65 70 75 80
 50 Leu Ala Ala Lys Leu Gly Gln Asp Val Val Phe Pro Gly Val Thr Arg
 85 90 95
 55 Gly Ala Glu Leu Glu Ala Ala Ile Asn Ala Leu Glu Asp Gly Gln Val
 100 105 110
 Leu Leu Val Glu Asn Thr Arg Tyr Glu Asp Val Asp Gly Lys Lys Glu

	115	120	125
5	Ser Lys Asn Asp Pro Glu Leu Gly Lys Tyr Trp Ala Ser Leu Gly Asp 130 135 140		
	Gly Ile Phe Val Asn Asp Ala Phe Gly Thr Ala His Arg Ala His Ala 145 150 155 160		
10	Ser Asn Val Gly Ile Ser Ala Asn Val Glu Lys Ala Val Ala Gly Phe 165 170 175		
	Leu Leu Glu Asn Glu Ile Ala Tyr Ile Gln Glu Ala Val Glu Thr Pro 180 185 190		
15	Glu Arg Pro Phe Val Ala Ile Leu Gly Gly Ser Lys Val Ser Asp Lys 195 200 205		
	Ile Gly Val Ile Glu Asn Leu Leu Glu Lys Ala Asp Lys Val Leu Ile 210 215 220		
20	Gly Gly Gly Met Thr Tyr Thr Phe Tyr Lys Ala Gln Gly Ile Glu Ile 225 230 235 240		
	Gly Asn Ser Leu Val Glu Glu Asp Lys Leu Asp Val Ala Lys Ala Leu 245 250 255		
25	Leu Glu Lys Ala Asn Gly Lys Leu Ile Leu Pro Val Asp Ser Lys Glu 260 265 270		
30	Ala Asn Ala Phe Ala Gly Tyr Thr Glu Val Arg Asp Thr Glu Gly Glu 275 280 285		
	Ala Val Ser Glu Gly Phe Leu Gly Leu Asp Ile Gly Pro Lys Ser Ile 290 295 300		
35	Ala Lys Phe Asp Glu Ala Leu Thr Gly Ala Lys Thr Val Val Trp Asn 305 310 315 320		
	Gly Pro Met Gly Val Phe Glu Asn Pro Asp Phe Gln Ala Gly Thr Ile 325 330 335		
40	Gly Val Met Asp Ala Ile Val Lys Gln Pro Gly Val Lys Ser Ile Ile 340 345 350		
45	Gly Gly Gly Asp Ser Ala Ala Ala Ile Asn Leu Gly Arg Ala Asp 355 360 365		
	Lys Phe Ser Trp Ile Ser Thr Gly Gly Gly Ala Ser Met Glu Leu Leu 370 375 380		
50	Glu Gly Lys Val Leu Pro Gln Leu Ala Ala Leu Thr Glu Lys 385 390 395		
55	<210> 179 <211> 165 <212> PRT		

<213> Streptococcus pneumoniae

<400> 179

5 Met Leu Lys Ser Glu Lys Gln Ser Arg Tyr Gln Met Leu Asn Glu Glu
 1 5 10 15
 Leu Ser Phe Leu Leu Glu Gly Glu Thr Asn Val Leu Ala Asn Leu Ser
 20 25 30
 10 Asn Ala Ser Ala Leu Ile Lys Ser Arg Phe Pro Asn Thr Val Phe Ala
 35 40 45
 Gly Phe Tyr Leu Phe Asp Gly Lys Glu Leu Val Leu Gly Pro Phe Gln
 50 55 60
 15 Gly Gly Val Ser Cys Ile Arg Ile Ala Leu Gly Lys Gly Val Cys Gly
 65 70 75 80
 20 Glu Ala Ala His Phe Gln Glu Thr Val Ile Val Gly Asp Val Thr Thr
 85 90 95
 Tyr Leu Asn Tyr Ile Ser Cys Asp Ser Leu Ala Lys Ser Glu Ile Val
 100 105 110
 25 Val Pro Met Met Lys Asn Gly Gln Leu Leu Gly Val Leu Asp Leu Asp
 115 120 125
 Ser Ser Glu Ile Glu Asp Tyr Asp Ala Met Asp Arg Asp Tyr Leu Glu
 130 135 140
 30 Gln Phe Val Ala Ile Leu Leu Glu Lys Thr Ala Trp Asp Phe Thr Met
 145 150 155 160
 35 Phe Glu Glu Lys Ser
 165

<210> 180

<211> 209

40 <212> PRT

<213> Streptococcus pneumoniae

<400> 180

45 Met Thr Ile Glu Leu Leu Thr Pro Phe Thr Lys Val Glu Leu Glu Pro
 1 5 10 15
 Glu Ile Lys Glu Lys Lys Arg Lys Gln Val Gly Ile Leu Gly Gly Asn
 20 25 30
 50 Phe Asn Pro Val His Asn Ala His Leu Ile Val Ala Asp Gln Val Arg
 35 40 45
 Gln Gln Leu Gly Leu Asp Gln Val Leu Leu Met Pro Glu Tyr Gln Pro
 50 55 60
 55 Pro His Val Asp Lys Lys Glu Thr Ile Pro Glu His His Arg Leu Lys
 65 70 75 80

Met Leu Glu Leu Ala Ile Glu Gly Ile Asp Gly Leu Val Ile Glu Thr
 85 90 95
 5 Ile Glu Leu Glu Arg Lys Gly Ile Ser Tyr Thr Tyr Asp Thr Met Lys
 100 105 110
 Ile Leu Thr Glu Lys Asn Pro Asp Thr Asp Tyr Tyr Phe Ile Ile Gly
 115 120 125
 10 Ala Asp Met Val Asp Tyr Leu Pro Lys Trp Tyr Arg Ile Asp Glu Leu
 130 135 140
 Val Asp Met Val Gln Phe Val Gly Val Gln Arg Pro Arg Tyr Lys Val
 145 150 155 160
 15 Gly Thr Ser Tyr Pro Val Ile Trp Val Asp Val Pro Leu Met Asp Ile
 165 170 175
 20 Ser Ser Ser Met Val Arg Ala Phe Leu Ala Gln Gly Arg Lys Pro Asn
 180 185 190
 Phe Leu Leu Pro Gln Pro Val Leu Asp Tyr Ile Glu Lys Glu Gly Leu
 195 200 205
 25 Tyr
 30 <210> 181
 <211> 255
 <212> PRT
 <213> Streptococcus pneumoniae
 35 <400> 181
 Met Asn Ile Ala Lys Ile Val Arg Glu Ala Arg Glu Gln Ser Arg Leu
 1 5 10 15
 Thr Thr Leu Asp Phe Ala Thr Gly Ile Phe Asp Glu Phe Ile Gln Leu
 20 25 30
 His Gly Asp Arg Ser Phe Arg Asp Asp Gly Ala Val Val Gly Gly Ile
 35 40 45
 45 Gly Trp Leu Gly Asp Gln Ala Val Thr Val Val Gly Ile Gln Lys Gly
 50 55 60
 Lys Ser Leu Gln Asp Asn Leu Lys Arg Asn Phe Gly Gln Pro His Pro
 65 70 75 80
 50 Glu Gly Tyr Arg Lys Ala Leu Arg Leu Met Lys Gln Ala Glu Lys Phe
 85 90 95
 Gly Arg Pro Val Val Thr Phe Ile Asn Thr Ala Gly Ala Tyr Pro Gly
 100 105 110
 55 Val Gly Ala Glu Glu Arg Gly Gln Gly Glu Ala Ile Ala Arg Asn Leu

	115	120	125
5	Met Glu Met Ser Asp Leu Lys Val Pro Ile Ile Ala Ile Ile Ile Gly 130 135 140		
	Glu Gly Gly Ser Gly Gly Ala Leu Ala Leu Ala Val Ala Asp Arg Val 145 150 155 160		
10	Trp Met Leu Glu Asn Ser Ile Tyr Ala Ile Leu Ser Pro Glu Gly Phe 165 170 175		
	Ala Ser Ile Leu Trp Lys Asp Gly Thr Arg Ala Met Glu Ala Ala Glu 180 185 190		
15	Leu Met Lys Ile Thr Ser His Glu Leu Leu Glu Met Asp Val Val Asp 195 200 205		
	Lys Val Ile Ser Glu Val Gly Leu Ser Ser Lys Glu Leu Ile Lys Ser 210 215 220		
20	Val Lys Lys Glu Leu Gln Thr Glu Leu Ala Arg Leu Ser Gln Lys Pro 225 230 235 240		
	Leu Glu Glu Leu Leu Glu Glu Arg Tyr Gln Arg Phe Arg Lys Tyr 245 250 255		
25			
	<210> 182 <211> 169 <212> PRT <213> Streptococcus pneumoniae		
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	<400> 182 Met Ile Ile Lys Val Glu Met Ala Asp Val Glu Val Leu Ala Lys Ile 1 5 10 15		
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	Ala Lys Gln Thr Phe Arg Glu Thr Phe Ala Tyr Asp Asn Thr Glu Glu 20 25 30		
40			
	Gln Leu Gln Glu Tyr Phe Glu Glu Ala Tyr Ser Leu Lys Thr Leu Ser 35 40 45		
	Thr Glu Leu Gly Asn Pro Asp Ser Glu Thr Tyr Phe Ile Met His Glu 50 55 60		
45			
	Glu Glu Ile Ala Gly Phe Leu Lys Val Asn Trp Gly Ser Ala Gln Thr 65 70 75 80		
	Glu Arg Glu Leu Glu Asp Ala Phe Glu Ile Gln Arg Leu Tyr Val Leu 85 90 95		
50			
	Gln Lys Phe Gln Gly Phe Gly Leu Gly Lys Gln Leu Phe Glu Phe Ala 100 105 110		
55			
	Leu Glu Leu Ala Thr Lys Asn Ser Phe Ser Trp Ala Trp Leu Gly Val 115 120 125		

Trp Glu His Asn Thr Lys Ala Gln Ala Phe Tyr Asn Arg Tyr Gly Phe
 130 135 140

5 Glu Lys Phe Ser Gln His His Phe Met Val Gly Gln Lys Val Asp Thr
 145 150 155 160

Asp Trp Leu Leu Arg Lys Lys Leu Arg
 165

10 <210> 183
 <211> 529
 <212> PRT
 <213> Streptococcus pneumoniae

15 <400> 183
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 1 5 10 15

20 Leu Leu Gly Ala Val Tyr Ile Ile Pro Trp Tyr Ile Trp Met Gly Ala
 20 25 30

Tyr Ala Ala Lys Ala Asn Gly Leu Phe Thr Met Gly Tyr Thr Ile Tyr
 35 40 45

25 Ala Trp Phe Leu Leu Val Ser Thr Ala Gly Ile Pro Val Ala Val Ala
 50 55 60

30 Lys Gln Val Ala Lys Tyr Asn Thr Met Arg Glu Glu Glu His Ser Phe
 65 70 75 80

Ala Leu Ile Arg Ser Phe Leu Gly Phe Met Thr Gly Leu Gly Leu Val
 85 90 95

35 Phe Ala Leu Val Leu Tyr Val Phe Ala Pro Trp Leu Ala Asp Leu Ser
 100 105 110

Gly Val Gly Lys Asp Leu Ile Pro Ile Met Gln Ser Leu Ala Trp Gly
 115 120 125

40 Val Leu Ile Phe Pro Ser Met Ser Val Ile Arg Gly Phe Phe Gln Gly
 130 135 140

45 Met Asn Asn Leu Lys Pro Tyr Ala Met Ser Gln Ile Ala Glu Gln Val
 145 150 155 160

Ile Arg Val Ile Trp Met Leu Leu Ala Thr Phe Ile Ile Met Lys Leu
 165 170 175

50 Gly Ser Gly Asp Tyr Leu Ala Ala Val Thr Gln Ser Thr Phe Ala Ala
 180 185 190

Phe Val Gly Met Val Ala Ser Phe Ala Val Leu Ile Tyr Phe Leu Ala
 195 200 205

55 Gln Glu Ser Ser Leu Lys Arg Val Phe Glu Thr Gly Asp Lys Ile Asn
 210 215 220

	Ser	Lys	Arg	Leu	Leu	Val	Asp	Thr	Ile	Lys	Glu	Ala	Ile	Pro	Phe	Ile	225		230		235				240
5	Leu	Thr	Gly	Ser	Ala	Ile	Gln	Ile	Phe	Gln	Ile	Leu	Asp	Gln	Leu	Thr		245		250				255	
	Phe	Ile	Asn	Ser	Met	Ser	Trp	Phe	Thr	Asn	Tyr	Ser	Asn	Glu	Asp	Leu	260		265				270		
10	Val	Val	Met	Phe	Ser	Tyr	Phe	Ser	Ala	Asn	Pro	Asn	Lys	Ile	Thr	Met		275		280			285		
15	Ile	Leu	Ile	Ser	Val	Gly	Val	Ser	Ile	Gly	Ser	Val	Gly	Leu	Pro	Leu	290		295			300			
	Leu	Thr	Glu	Asn	Tyr	Val	Lys	Gly	Asp	Leu	Lys	Ala	Ala	Ser	Arg	Leu	305		310		315		320		
20	Val	Gln	Asp	Ser	Leu	Thr	Leu	Leu	Phe	Met	Phe	Leu	Leu	Pro	Ala	Thr		325		330			335		
	Val	Gly	Val	Val	Met	Val	Gly	Glu	Pro	Leu	Tyr	Thr	Val	Phe	Tyr	Gly		340		345			350		
25	Lys	Pro	Asp	Ser	Leu	Ala	Leu	Gly	Leu	Phe	Val	Phe	Ala	Val	Leu	Gln		355		360			365		
30	Ser	Ile	Ile	Leu	Gly	Leu	Tyr	Met	Val	Leu	Ser	Pro	Met	Leu	Gln	Ala	370		375			380			
	Met	Phe	Arg	Asn	Arg	Lys	Ala	Val	Leu	Tyr	Phe	Ile	Tyr	Gly	Ser	Ile	385		390		395		400		
35	Ala	Lys	Leu	Val	Leu	Gln	Leu	Pro	Thr	Ile	Ala	Leu	Phe	His	Ser	Tyr		405		410			415		
	Gly	Pro	Leu	Ile	Ser	Thr	Thr	Ile	Ala	Leu	Ile	Ile	Pro	Asn	Val	Leu		420		425			430		
40	Met	Tyr	Arg	Asp	Ile	Cys	Lys	Val	Thr	Gly	Val	Lys	Arg	Lys	Val	Ile		435		440			445		
45	Leu	Lys	Arg	Thr	Ile	Leu	Ile	Ser	Leu	Leu	Thr	Leu	Val	Met	Phe	Leu	450		455			460			
	Leu	Ile	Gly	Thr	Ile	Gln	Trp	Leu	Leu	Gly	Phe	Phe	Phe	Gln	Pro	Ser	465		470		475		480		
50	Gly	Arg	Leu	Trp	Ser	Phe	Phe	Tyr	Val	Ala	Leu	Val	Gly	Ala	Met	Gly		485		490			495		
	Gly	Gly	Leu	Tyr	Met	Val	Met	Ser	Leu	Arg	Thr	Tyr	Leu	Leu	Asp	Lys		500		505			510		
55	Val	Ile	Gly	Lys	Ala	Gln	Ala	Asp	Arg	Leu	Arg	Ala	Lys	Phe	Lys	Leu	515		520			525			

Ser

5

<210> 184

<211> 155

<212> PRT

<213> Streptococcus pneumoniae

10

<400> 184

Met	Ser	Asp	Lys	Ile	Gly	Leu	Phe	Thr	Gly	Ser	Phe	Asp	Pro	Met	Thr
1				5					10					15	

15

Asn	Gly	His	Leu	Asp	Ile	Ile	Glu	Arg	Ala	Ser	Arg	Leu	Phe	Asp	Lys
			20					25					30		

Leu	Tyr	Val	Gly	Ile	Phe	Phe	Asn	Pro	His	Lys	Gln	Gly	Phe	Leu	Pro
		35					40					45			

20

Ile	Glu	Asn	Arg	Lys	Arg	Gly	Leu	Glu	Lys	Ala	Leu	Gly	His	Leu	Glu
	50					55					60				

25

Asn	Val	Glu	Val	Val	Ala	Ser	His	Asp	Glu	Leu	Val	Val	Asp	Val	Ala
65					70					75					80

Lys	Arg	Leu	Gly	Ala	Thr	Cys	Leu	Val	Arg	Gly	Leu	Arg	Asn	Ala	Ser
			85						90					95	

30

Asp	Leu	Gln	Tyr	Glu	Ala	Ser	Phe	Asp	Tyr	Tyr	Asn	His	Gln	Leu	Ser
			100					105					110		

Ser	Asp	Ile	Glu	Thr	Ile	Tyr	Leu	His	Ser	Arg	Pro	Glu	His	Leu	Tyr
		115					120					125			

35

Ile	Ser	Ser	Ser	Gly	Val	Arg	Glu	Leu	Leu	Lys	Phe	Gly	Gln	Asp	Ile
	130					135					140				

40

Ala	Cys	Tyr	Val	Pro	Glu	Ser	Ile	Trp	Arg	Lys
145					150					155

<210> 185

<211> 143

<212> PRT

<213> Streptococcus pneumoniae

45

<400> 185

Met	Thr	Ile	Leu	Phe	Val	Val	Ile	Ser	Ala	Ser	Phe	Leu	Tyr	Met	Val
1				5					10					15	

50

Ser	Leu	Ser	Met	Lys	Pro	Tyr	Gln	Thr	Ala	Lys	Ser	Glu	Gly	Glu	Lys
			20					25					30		

55

Leu	Ala	Gln	Gln	Tyr	Ala	Gly	Leu	Glu	Gln	Ala	Asp	Gln	Val	Asp	Leu
		35					40					45			

Tyr Asn Gly Leu Glu Ser Tyr Tyr Ser Val Leu Gly Arg Asn Lys Gln
 50 55 60
 5 Gln Glu Ala Leu Ala Val Leu Ile Gly Lys Asp Asp His Lys Ile Tyr
 65 70 75 80
 Val Tyr Gln Leu Asn Gln Gly Val Ser Gln Glu Lys Ala Glu Thr Val
 85 90 95
 10 Ser Lys Glu Lys Gly Ala Gly Glu Ile Asp Lys Ile Ile Phe Gly Arg
 100 105 110
 Tyr Gln Asp Lys Pro Ile Trp Glu Val Lys Ser Gly Ser Asp Phe Tyr
 115 120 125
 15 Leu Val Asp Phe Glu Thr Gly Ala Leu Val Asn Lys Glu Gly Leu
 130 135 140
 20 <210> 186
 <211> 243
 <212> PRT
 <213> Streptococcus pneumoniae
 25 <400> 186
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 30 Lys Ser Arg Glu Glu Ser Lys Ala Leu Leu Thr Glu Ala Tyr Arg Gln
 20 25 30
 Gly Val Arg Thr Ile Val Ser Thr Ser His Arg Arg Lys Gly Met Phe
 35 40 45
 35 Glu Thr Pro Glu Glu Lys Ile Ala Glu Asn Phe Leu Gln Val Arg Glu
 50 55 60
 Ile Ala Lys Glu Val Ala Ser Asp Leu Val Ile Ala Tyr Gly Ala Glu
 65 70 75 80
 40 Ile Tyr Tyr Thr Pro Asp Val Leu Asp Lys Leu Glu Asn Asn Arg Ile
 85 90 95
 Pro Thr Leu Asn Asn Ser Arg Tyr Ala Leu Ile Glu Phe Ser Met Asn
 100 105 110
 45 Thr Pro Tyr Arg Asp Ile His Ser Ala Leu Asn Lys Ile Leu Met Leu
 115 120 125
 50 Gly Ile Thr Pro Val Ile Ala His Ile Glu Arg Tyr Asp Val Leu Glu
 130 135 140
 Asn Asn Glu Lys Arg Val Arg Glu Leu Ile Asp Met Gly Cys Tyr Thr
 145 150 155 160
 55 Gln Ile Asn Ser Ser His Val Leu Lys Ser Lys Leu Phe Gly Glu Pro
 165 170 175

Tyr Lys Phe Met Lys Lys Arg Ala Gln Tyr Phe Leu Glu Arg Asp Leu
 180 185 190
 5 Val His Ile Ile Ala Ser Asp Met His Asn Val Asp Gly Arg Pro Pro
 195 200 205
 His Met Ala Glu Ala Tyr Asp Leu Val Ser Gln Lys Tyr Gly Glu Ala
 210 215 220
 10 Lys Ala Gln Glu Leu Phe Ile Asp Asn Pro Arg Lys Ile Val Met Asp
 225 230 235 240
 Gln Leu Ile
 15
 <210> 187
 <211> 308
 20 <212> PRT
 <213> Streptococcus pneumoniae
 <400> 187
 25 Met Ser Thr Ile Asp Lys Glu Lys Phe Gln Phe Val Lys Arg Asp Asp
 1 5 10 15
 Phe Ala Ser Glu Thr Ile Asp Ala Pro Ala Tyr Ser Tyr Trp Lys Ser
 20 25 30
 30 Val Phe Lys Gln Phe Met Lys Lys Lys Ser Thr Val Val Met Leu Gly
 35 40 45
 Ile Leu Val Ala Ile Ile Leu Ile Ser Phe Ile Tyr Pro Met Phe Ser
 50 55 60
 35 Lys Phe Asp Phe Asn Asp Val Ser Lys Val Asn Asp Phe Ser Val Arg
 65 70 75 80
 40 Tyr Ile Lys Pro Asn Ala Glu His Trp Phe Gly Thr Asp Ser Asn Gly
 85 90 95
 Lys Ser Leu Phe Asp Gly Val Trp Phe Gly Ala Arg Asn Ser Ile Leu
 100 105 110
 45 Ile Ser Val Ile Ala Thr Val Ile Asn Leu Val Ile Gly Val Phe Val
 115 120 125
 Gly Gly Ile Trp Gly Ile Ser Lys Ser Val Asp Arg Val Met Met Glu
 130 135 140
 50 Val Tyr Asn Val Ile Ser Asn Ile Pro Pro Leu Leu Ile Val Ile Val
 145 150 155 160
 55 Leu Thr Tyr Ser Ile Gly Ala Gly Phe Trp Asn Leu Ile Phe Ala Met
 165 170 175
 Ser Val Thr Thr Trp Ile Gly Ile Ala Phe Met Ile Arg Val Gln Ile

	180	185	190
	Leu Arg Tyr Arg Asp Leu Glu Tyr Asn Leu Ala Ser Arg Thr Leu Gly		
	195	200	205
5	Thr Pro Thr Leu Lys Ile Val Ala Lys Asn Ile Met Pro Gln Leu Val		
	210	215	220
10	Ser Val Ile Val Thr Thr Met Thr Gln Met Leu Pro Ser Phe Ile Ser		
	225	230	235
	Tyr Glu Ala Phe Leu Ser Phe Phe Gly Leu Gly Leu Pro Ile Thr Val		
	245	250	255
15	Pro Ser Leu Gly Arg Leu Ile Ser Asp Tyr Ser Gln Asn Val Thr Thr		
	260	265	270
	Asn Ala Tyr Leu Phe Trp Ile Pro Leu Thr Thr Leu Val Leu Val Ser		
	275	280	285
20	Leu Ser Leu Phe Val Val Gly Gln Asn Leu Ala Asp Ala Ser Asp Pro		
	290	295	300
25	Arg Thr His Arg		
	305		
	<210> 188		
	<211> 77		
30	<212> PRT		
	<213> Streptococcus pneumoniae		
	<400> 188		
35	Met Tyr Asn Leu Leu Leu Thr Ile Leu Leu Val Leu Ser Val Val Ile		
	1	5	10
	Val Ile Ala Ile Phe Met Gln Pro Thr Lys Asn Gln Ser Ser Asn Val		
	20	25	30
40	Phe Asp Ala Ser Ser Gly Asp Leu Phe Glu Arg Ser Lys Ala Arg Gly		
	35	40	45
	Phe Glu Ala Val Met Gln Arg Leu Thr Gly Ile Leu Val Phe Phe Trp		
	50	55	60
45	Leu Ala Ile Ala Leu Ala Leu Thr Val Leu Ser Ser Arg		
	65	70	75
50	<210> 189		
	<211> 369		
	<212> PRT		
	<213> Streptococcus pneumoniae		
55	<400> 189		
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	1	5	10
			15

	Leu	Thr	Ile	Ile	Phe	Tyr	Leu	Trp	Arg	Gln	Met	Gly	Ser	Leu	Ile	Asn
				20					25					30		
5	Pro	Phe	Val	Ser	Val	Leu	Asn	Thr	Ile	Met	Ile	Pro	Phe	Leu	Leu	Gly
			35					40					45			
	Gly	Phe	Leu	Tyr	Tyr	Leu	Thr	Asn	Pro	Ile	Val	Thr	Phe	Leu	Asn	Lys
		50					55					60				
10	Val	Cys	Lys	Leu	Asn	Arg	Leu	Leu	Gly	Ile	Leu	Ile	Thr	Leu	Cys	Thr
	65					70					75					80
	Leu	Val	Trp	Gly	Met	Val	Ile	Gly	Val	Val	Tyr	Leu	Leu	Pro	Ile	Leu
15					85					90					95	
	Ile	Asn	Gln	Leu	Ser	Ser	Leu	Ile	Ile	Ser	Ser	Gln	Thr	Ile	Tyr	Ser
				100					105					110		
20	Arg	Val	Gln	Asp	Leu	Ile	Ile	Asp	Leu	Ser	Asn	Tyr	Pro	Ala	Leu	Gln
			115					120					125			
	Asn	Leu	Asp	Val	Glu	Ala	Thr	Ile	Gln	Gln	Leu	Asn	Leu	Ser	Tyr	Val
25		130					135					140				
	Asp	Ile	Leu	Gln	Asn	Ile	Leu	Asn	Ser	Val	Ser	Asn	Ser	Val	Gly	Ser
	145					150					155					160
	Val	Leu	Ser	Ala	Leu	Ile	Ser	Thr	Val	Leu	Ile	Leu	Ile	Met	Thr	Pro
30					165					170					175	
	Val	Phe	Leu	Val	Tyr	Phe	Leu	Leu	Asp	Gly	His	Lys	Phe	Leu	Pro	Met
				180					185					190		
35	Leu	Glu	Arg	Thr	Ile	Leu	Lys	Arg	Asp	Arg	Leu	His	Ile	Ala	Gly	Leu
			195					200					205			
	Leu	Lys	Asn	Leu	Asn	Ala	Thr	Ile	Ala	Arg	Tyr	Ile	Ser	Gly	Val	Ser
40		210					215					220				
	Ile	Asp	Ala	Ile	Ile	Ile	Gly	Cys	Leu	Ala	Tyr	Ile	Gly	Tyr	Ser	Ile
	225					230					235					240
	Ile	Gly	Leu	Lys	Tyr	Ala	Leu	Val	Phe	Ala	Ile	Phe	Ser	Gly	Val	Ala
45					245					250					255	
	Asn	Leu	Ile	Pro	Tyr	Val	Gly	Pro	Ser	Ile	Gly	Leu	Ile	Pro	Met	Ile
				260					265					270		
50	Ile	Ala	Asn	Ile	Phe	Thr	Val	Pro	His	Arg	Leu	Leu	Ile	Ala	Val	Ile
			275					280					285			
	Tyr	Met	Leu	Val	Val	Gln	Gln	Val	Asp	Gly	Asn	Ile	Leu	Tyr	Pro	Arg
55		290					295					300				
	Ile	Val	Gly	Ser	Val	Met	Lys	Val	His	Pro	Ile	Thr	Ile	Leu	Val	Leu
	305					310					315					320

Leu Leu Leu Ser Ser Asn Ile Tyr Gly Val Val Gly M t Ile Val Ala
 325 330 335
 5 Val Pro Thr Tyr Ser Ile Leu Lys Glu Ile Ser Lys Phe Leu Ser Arg
 340 345 350
 Leu Tyr Glu Asn His Lys Ile Met Lys Glu Arg Glu Arg Glu Leu Ala
 355 360 365
 10 Lys
 15 <210> 190
 <211> 451
 <212> PRT
 <213> Streptococcus pneumoniae
 20 <400> 190
 Met Tyr Gln Ala Leu Tyr Arg Lys Tyr Arg Ser Gln Asn Phe Ser Gln
 1 5 10 15
 Leu Val Gly Gln Glu Val Val Ala Lys Thr Leu Lys Gln Ala Val Glu
 20 25 30
 Gln Glu Lys Ile Ser His Ala Tyr Leu Phe Ser Gly Pro Arg Gly Thr
 35 40 45
 30 Gly Lys Thr Ser Val Ala Lys Ile Phe Ala Lys Ala Met Asn Cys Pro
 50 55 60
 Asn Gln Val Gly Gly Glu Pro Cys Asn Asn Cys Tyr Ile Cys Gln Ala
 65 70 75 80
 35 Val Thr Asp Gly Ser Leu Glu Asp Val Ile Glu Met Asp Ala Ala Ser
 85 90 95
 Asn Asn Gly Val Asp Glu Ile Arg Glu Ile Arg Asp Lys Ser Thr Tyr
 100 105 110
 Ala Pro Ser Leu Ala Arg Tyr Lys Val Tyr Ile Ile Asp Glu Val His
 115 120 125
 45 Met Leu Ser Thr Gly Ala Phe Asn Ala Leu Leu Lys Thr Leu Glu Glu
 130 135 140
 Pro Thr Gln Asn Val Val Phe Ile Leu Ala Thr Thr Glu Leu His Lys
 145 150 155 160
 50 Ile Pro Ala Thr Ile Leu Ser Arg Val Gln Arg Phe Glu Phe Lys Ser
 165 170 175
 Ile Lys Thr Gln Asp Ile Lys Glu His Ile His Tyr Ile Leu Glu Lys
 180 185 190
 55 Glu Asn Ile Ser Ser Glu Pro Glu Ala Val Glu Ile Ile Ala Arg Arg

	195	200	205
5	Ala Glu Gly Gly Met Arg Asp 210	Ala Leu Ser Ile Leu Asp 215 220	Gln Ala Leu
	Ser Leu Thr Gln Gly Asn Glu Leu Thr Thr 225 230	Ala Ile Ser Glu Glu Ile 235 240	
10	Thr Gly Thr Ile Ser Leu Ser Ala Leu Asp Asp Tyr Val Ala Ala Leu 245 250 255		
	Ser Gln Gln Asp Val Pro Lys Ala Leu Ser Cys Leu Asn Leu Leu Phe 260 265 270		
15	Asp Asn Gly Lys Ser Met Thr Arg Phe Val Thr Asp Leu Leu His Tyr 275 280 285		
20	Leu Arg Asp Leu Leu Ile Val Gln Thr Gly Gly Glu Asn Thr His His 290 295 300		
	Ser Ser Val Phe Val Glu Asn Leu Ala Leu Pro Gln Lys Asn Leu Phe 305 310 315 320		
25	Glu Met Ile Arg Leu Ala Thr Val Asn Leu Ala Asp Ile Lys Ser Ser 325 330 335		
	Leu Gln Pro Lys Ile Tyr Ala Glu Met Met Thr Val Arg Leu Ala Glu 340 345 350		
30	Ile Lys Pro Glu Pro Ala Leu Ser Gly Ala Val Glu Asn Glu Ile Ala 355 360 365		
35	Thr Leu Arg Gln Glu Val Ala Arg Leu Lys Gln Glu Leu Ser Asn Ala 370 375 380		
	Gly Ala Val Pro Lys Gln Val Ala Pro Ala Pro Ser Arg Pro Ala Thr 385 390 395 400		
40	Gly Lys Thr Val Tyr Arg Val Asp Arg Asn Lys Val Gln Ser Ile Leu 405 410 415		
	Gln Glu Ala Val Glu Asn Pro Asp Leu Thr Arg Gln Asn Leu Ile Arg 420 425 430		
45	Leu Gln Asn Ala Trp Gly Glu Val Ile Glu Ser Leu Gly Gly Pro Asp 435 440 445		
50	Lys Leu Cys 450		
55	<210> 191 <211> 662 <212> PRT <213> Streptococcus pneumoniae <400> 191		

	Met	Phe	Arg	Leu	Thr	Asn	Lys	Leu	Ala	Val	Ser	Asn	Leu	Ile	Lys	Asn	
	1				5					10					15		
5	Arg	Lys	Leu	Tyr	Tyr	Pro	Phe	Ala	Leu	Ala	Val	L u	Leu	Ala	Val	Thr	
				20					25					30			
	Leu	Thr	Tyr	Leu	Phe	Tyr	Ser	Leu	Thr	Phe	Asn	Pro	Lys	Ile	Ala	Glu	
			35					40					45				
10	Ile	Arg	Gly	Gly	Thr	Thr	Ile	Gln	Ala	Thr	Leu	Gly	Phe	Gly	Met	Phe	
		50					55					60					
	Val	Val	Thr	Leu	Ala	Ser	Ala	Ile	Ile	Val	Leu	Tyr	Ala	Asn	Ser	Phe	
	65					70					75					80	
15	Val	Met	Lys	Lys	Arg	Ser	Lys	Glu	Leu	Gly	Ile	Tyr	Gly	Met	Leu	Gly	
					85					90					95		
	Leu	Glu	Lys	Arg	His	Leu	Ile	Ser	Met	Thr	Phe	Lys	Glu	Leu	Val	Val	
20				100					105					110			
	Phe	Gly	Ile	Leu	Thr	Val	Gly	Ala	Gly	Ile	Gly	Ile	Gly	Ala	Leu	Phe	
			115					120					125				
25	Asp	Lys	Leu	Ile	Phe	Ala	Phe	Leu	Leu	Lys	Leu	Met	Lys	Leu	Lys	Val	
		130					135					140					
	Glu	Leu	Val	Ala	Thr	Phe	Gln	Thr	Lys	Val	Val	Ile	Thr	Val	Leu	Val	
	145					150					155					160	
30	Val	Phe	Gly	Leu	Ile	Phe	Leu	Gly	Leu	Met	Phe	Leu	Asn	Ala	Leu	Arg	
					165					170					175		
	Ile	Ala	Arg	Met	Asn	Ala	Leu	Gln	Leu	Ser	Arg	Glu	Lys	Ala	Ser	Gly	
35				180					185					190			
	Glu	Lys	Lys	Gly	Arg	Phe	Leu	Pro	Leu	Gln	Thr	Ile	Leu	Gly	Ser	Ile	
			195					200					205				
40	Ser	Leu	Gly	Ile	Gly	Tyr	Tyr	Leu	Ala	Leu	Thr	Val	Lys	Asp	Pro	Leu	
		210					215					220					
	Thr	Ala	Leu	Thr	Thr	Phe	Phe	Ile	Ala	Val	Leu	Leu	Val	Ile	Phe	Gly	
	225					230					235					240	
45	Thr	Tyr	Leu	Leu	Phe	Asn	Ala	Gly	Ile	Thr	Val	Phe	Leu	Gln	Ile	Leu	
					245					250					255		
	Lys	Lys	Asn	Lys	Lys	Tyr	Tyr	Tyr	Gln	Pro	Asn	Asn	Leu	Ile	Ser	Val	
50				260					265					270			
	Ser	Asn	Leu	Ile	Phe	Arg	Met	Lys	Lys	Asn	Ala	Val	Gly	Leu	Ala	Thr	
			275					280					285				
55	Ile	Ala	Ile	Leu	Ser	Thr	Met	Val	Leu	Val	Thr	Met	Ser	Ala	Ala	Thr	
		290					295					300					

	Ser	Ile	Phe	Asn	Ser	Ala	Glu	Ser	Phe	Lys	Lys	Val	Leu	Asn	Pro	His	
	305					310					315					320	
5	Asp	Phe	Gly	Val	Ser	Gly	Gln	Asn	Val	Glu	Lys	Glu	Asp	Leu	Asp	Lys	
					325					330					335		
	Leu	Leu	Ser	Gln	Phe	Ala	Ser	Asp	Asn	Gly	Tyr	Lys	Ile	Lys	Glu	Lys	
				340					345					350			
10	Glu	Val	Phe	Arg	Tyr	Thr	Tyr	Phe	Gly	Val	Ala	Asn	Gln	Glu	Gly	Asn	
			355					360					365				
	Lys	Leu	Thr	Phe	Phe	Glu	Lys	Gly	Gln	Asn	Arg	Val	Gln	Pro	Thr	Thr	
	370						375					380					
15	Val	Phe	Met	Val	Phe	Asp	Gln	Lys	Asp	Tyr	Glu	Asn	Met	Thr	Gly	Gln	
	385					390					395					400	
	Lys	Leu	Ser	Leu	Ser	Gly	Asn	Glu	Val	Gly	Leu	Phe	Ala	Lys	Asn	Asp	
20					405					410					415		
	Gly	Leu	Lys	Gly	Gln	Lys	Thr	Leu	Ile	Leu	Asn	Asp	His	Gln	Phe	Ser	
				420					425					430			
25	Val	Lys	Glu	Glu	Phe	Asn	Lys	Asp	Phe	Ile	Val	Asn	His	Val	Pro	Asn	
			435					440					445				
	Gln	Phe	Asn	Ile	Leu	Thr	Ala	Asp	Tyr	Asn	Tyr	Leu	Val	Val	Pro	Asp	
	450						455					460					
30	Leu	Gln	Ala	Phe	Leu	Asn	Gln	Phe	Pro	Asp	Ser	Asp	Ile	Tyr	Asn	Gln	
	465					470					475					480	
	Phe	Tyr	Gly	Gly	Met	Asn	Val	Asn	Val	Ser	Glu	Glu	Glu	Gln	Leu	Lys	
35					485					490					495		
	Val	Ala	Glu	Glu	Tyr	Glu	Asn	Tyr	Leu	Asn	Gln	Phe	Asn	Ala	Gln	Leu	
				500					505					510			
40	Asp	Thr	Glu	Gly	Ser	Tyr	Val	Tyr	Gly	Ser	Asn	Leu	Ala	Asp	Ala	Ser	
			515					520					525				
	Ser	Gln	Met	Ser	Ala	Leu	Phe	Gly	Gly	Val	Phe	Phe	Ile	Gly	Ile	Phe	
	530						535					540					
45	Leu	Ser	Ile	Ile	Phe	Met	Val	Gly	Thr	Val	Leu	Val	Ile	Tyr	Tyr	Lys	
	545					550					555					560	
	Gln	Ile	Ser	Glu	Gly	Tyr	Glu	Asp	Arg	Glu	Arg	Phe	Ile	Ile	Leu	Gln	
50					565					570					575		
	Lys	Val	Gly	Leu	Asp	Gln	Lys	Gln	Ile	Lys	Gln	Thr	Ile	His	Lys	Gln	
				580					585					590			
55	Val	Leu	Thr	Val	Phe	Phe	Leu	Pro	Leu	Leu	Phe	Ala	Phe	Ile	His	Leu	
			595					600					605				

Ala Phe Ala Tyr His Met Leu Ser Leu Ile Leu Lys Val Ile Gly Val
 610 615 620
 5 Leu Asp Thr Thr Met Met Leu Ile Val Thr Leu Ser Ile Cys Ala Ile
 625 630 635 640
 Phe Leu Ile Ala Tyr Val Leu Ile Phe Met Ile Thr Ser Arg Ser Tyr
 645 650 655
 10 Arg Lys Ile Val Gln Met
 660
 15 <210> 192
 <211> 296
 <212> PRT
 <213> Streptococcus pneumoniae
 20 <400> 192
 Met Lys Gln Asp Gln Leu Lys Ala Trp Gln Pro Ala Gln Phe Asp Arg
 1 5 10 15
 Phe Val Arg Ile Leu Glu Gln Asp Gln Leu Asn His Ala Tyr Leu Phe
 20 25 30
 25 Ser Gly Phe Phe Gly Ser Leu Glu Met Ala Gln Phe Leu Ala Lys Ser
 35 40 45
 30 Leu Phe Cys Thr Asp Lys Val Gly Val Leu Pro Cys Glu Lys Cys Arg
 50 55 60
 Ser Cys Lys Leu Ile Glu Gln Glu Glu Phe Pro Asp Val Thr Leu Ile
 65 70 75 80
 35 Lys Pro Val Asn Gln Val Ile Lys Thr Glu Arg Ile Arg Glu Leu Val
 85 90 95
 Gly Gln Phe Ser Gln Ala Gly Ile Glu Ser Gln Gln Gln Val Phe Ile
 100 105 110
 40 Ile Glu Gln Ala Asp Lys Met His Pro Asn Ala Ala Asn Ser Leu Leu
 115 120 125
 45 Lys Val Ile Glu Glu Pro Gln Ser Glu Val Tyr Ile Phe Phe Leu Thr
 130 135 140
 Ser Asp Glu Glu Lys Met Leu Pro Thr Ile Arg Ser Arg Thr Gln Ile
 145 150 155 160
 50 Phe His Phe Lys Lys Gln Glu Glu Lys Leu Ile Leu Leu Leu Glu Gln
 165 170 175
 Met Gly Leu Val Lys Lys Lys Ala Thr Leu Leu Ala Lys Phe Ser Gln
 180 185 190
 55 Ser Arg Ala Glu Ala Glu Lys Leu Ala Asn Gln Ala Ser Phe Trp Thr
 195 200 205

Leu Val Asp Glu Ser Glu Arg Leu Leu Thr Trp Leu Val Ala Lys Lys
 210 215 220
 5 Lys Glu Ser Tyr Leu Gln Val Ala Lys Leu Ala Asn Leu Ala Asp Asp
 225 230 235 240
 Lys Glu Lys Gln Asp Gln Val Leu Arg Ile Leu Glu Val Leu Cys Gly
 245 250 255
 10 Gln Asp Leu Leu Gln Val Arg Val Arg Val Ile Leu Gln Asp Leu Leu
 260 265 270
 Glu Ala Arg Lys Met Trp Gln Ala Asn Val Ser Phe Gln Asn Ala Met
 15 275 280 285
 Glu Tyr Leu Val Leu Lys Glu Ile
 290 295
 20
 <210> 193
 <211> 204
 <212> PRT
 <213> Streptococcus pneumoniae
 25
 <400> 193
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 30 Ile Leu Ser Leu Leu Ala Leu Ser Arg Ile Phe Phe Trp Ser Asn Val
 20 25 30
 Arg Val Glu Gly His Ser Met Asp Pro Thr Leu Ala Asp Gly Glu Ile
 35 35 40 45
 Leu Phe Val Val Lys His Leu Pro Ile Asp Arg Phe Asp Ile Val Val
 50 55 60
 40 Ala His Glu Glu Asp Gly Asn Lys Asp Ile Val Lys Arg Val Ile Gly
 65 70 75 80
 Met Pro Gly Asp Thr Ile Arg Tyr Glu Asn Asp Lys Leu Tyr Ile Asn
 85 90 95
 45 Asp Lys Glu Thr Asp Glu Pro Tyr Leu Ala Asp Tyr Ile Lys Arg Phe
 100 105 110
 Lys Asp Asp Lys Leu Gln Ser Thr Tyr Ser Gly Lys Gly Phe Glu Gly
 115 120 125
 50 Asn Lys Gly Thr Phe Phe Arg Ser Ile Ala Gln Lys Ala Gln Ala Phe
 130 135 140
 55 Thr Val Asp Val Asn Tyr Asn Thr Asn Phe Ser Phe Thr Val Pro Glu
 145 150 155 160
 Gly Glu Tyr Leu Leu Leu Gly Asp Asp Arg Leu Val Ser Ser Asp Ser

165 170 175
 Arg His Val Gly Thr Phe Lys Ala Lys Asp Ile Thr Gly Glu Ala Lys
 180 185 190
 5 Phe Arg Phe Trp Pro Ile Thr Arg Ile Gly Thr Phe
 195 200
 10 <210> 194
 <211> 328
 <212> PRT
 <213> Streptococcus pneumoniae
 15 <400> 194
 Met Val Val Phe Thr Gly Ser Thr Val Glu Glu Ala Ile Gln Lys Gly
 1 5 10 15
 20 Leu Lys Glu Leu Asp Ile Pro Arg Met Lys Ala His Ile Lys Val Ile
 20 25 30
 Ser Arg Glu Lys Lys Gly Phe Leu Gly Leu Phe Gly Lys Lys Pro Ala
 35 40 45
 25 Gln Val Asp Ile Glu Ala Ile Ser Glu Thr Thr Val Val Lys Ala Asn
 50 55 60
 Gln Gln Val Val Lys Gly Val Pro Lys Lys Ile Asn Asp Leu Asn Glu
 65 70 75 80
 30 Pro Val Lys Thr Val Ser Glu Glu Thr Val Asp Leu Gly His Val Val
 85 90 95
 35 Asn Ala Ile Lys Lys Ile Glu Glu Glu Gly Gln Gly Ile Ser Asp Glu
 100 105 110
 Val Lys Ala Glu Ile Leu Lys His Glu Arg His Ala Ser Thr Ile Leu
 115 120 125
 40 Glu Glu Thr Gly His Ile Glu Ile Leu Asn Glu Leu Gln Ile Glu Glu
 130 135 140
 Ala Met Arg Glu Glu Ala Gly Ala Asp Asp Leu Glu Thr Glu Gln Asp
 145 150 155 160
 45 Gln Thr Glu Asn Gln Asp Leu Lys Glu Met Gly Leu Lys Val Glu Gln
 165 170 175
 50 Ser Tyr Asp Ile Ala Gln Val Ala Thr Asp Val Thr Ala Tyr Val Gln
 180 185 190
 Ala Ile Val Asp Asp Met Asp Val Glu Ala Thr Leu Ser Asn Asp Tyr
 195 200 205
 55 Asn Arg Arg Ser Ile Asn Leu Gln Ile Asp Thr Asn Glu Pro Gly Arg
 210 215 220

Ile Ile Gly Tyr His Gly Lys Val Leu Lys Ala Leu Gln Leu Leu Ala
 225 230 235 240
 5 Gln Asn Tyr Leu Tyr Asn Arg Tyr Ser Lys Thr Phe Tyr Val Thr Ile
 245 250 255
 Asn Val Asn Asp Tyr Val Glu His Arg Ala Glu Val Leu Gln Thr Tyr
 260 265 270
 10 Ala Gln Lys Leu Ala Asn Arg Val Leu Glu Glu Gly Arg Ser His Lys
 275 280 285
 Thr Asp Pro Met Ser Asn Ser Glu Arg Lys Ile Ile His Arg Ile Ile
 290 295 300
 15 Ser Arg Met Asp Gly Val Thr Ser Tyr Ser Glu Gly Asp Glu Pro Asn
 305 310 315 320
 20 Arg Tyr Val Val Val Asp Thr Glu
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 <210> 195
 <211> 460
 25 <212> PRT
 <213> Streptococcus pneumoniae
 <400> 195
 30 Met Ser Asn Phe Ala Ile Ile Leu Ala Ala Gly Lys Gly Thr Arg Met
 1 5 10 15
 Lys Ser Asp Leu Pro Lys Val Leu His Lys Val Ala Gly Ile Ser Met
 20 25 30
 35 Leu Glu His Val Phe Arg Ser Val Gly Ala Ile Gln Pro Glu Lys Thr
 35 40 45
 Val Thr Val Val Gly His Lys Ala Glu Leu Val Glu Glu Val Leu Ala
 50 55 60
 40 Gly Gln Thr Glu Phe Val Thr Gln Ser Glu Gln Leu Gly Thr Gly His
 65 70 75 80
 45 Ala Val Met Met Thr Glu Pro Ile Leu Glu Gly Val Ser Gly His Thr
 85 90 95
 Leu Val Ile Ala Gly Asp Thr Pro Leu Ile Thr Gly Glu Ser Leu Lys
 100 105 110
 50 Asn Leu Ile Asp Phe His Ile Asn His Lys Asn Val Ala Thr Ile Leu
 115 120 125
 Thr Ala Glu Thr Asp Asn Pro Phe Gly Tyr Gly Arg Ile Val Arg Asn
 130 135 140
 55 Asp Asn Ala Glu Val Leu Arg Ser Leu Leu Ser Arg Arg Met Leu Gln
 145 150 155 160

	Ile	Leu	Lys	Ser	Lys	Ser	Arg	Lys	Ser	Thr	Leu	Val	Thr	Tyr	Val	Phe
					165					170					175	
5	Asp	Asn	Glu	Arg	Leu	Phe	Glu	Ala	Leu	Lys	Asn	Ile	Asn	Thr	Asn	Asn
				180					185					190		
	Ala	Gln	Gly	Glu	Tyr	Tyr	Ile	Thr	Asp	Val	Ile	Gly	Ile	Phe	Arg	Glu
10			195					200					205			
	Thr	Gly	Glu	Lys	Val	Gly	Ala	Tyr	Thr	Leu	Lys	Asp	Phe	Asp	Glu	Ser
		210					215					220				
15	Leu	Gly	Val	Asn	Asp	Arg	Val	Ala	Leu	Ala	Thr	Ala	Glu	Ser	Val	Met
	225					230					235					240
	Arg	Arg	Arg	Ile	Asn	His	Lys	His	Met	Val	Asn	Gly	Val	Ser	Phe	Val
					245					250					255	
20	Asn	Pro	Glu	Ala	Thr	Tyr	Ile	Asp	Ile	Asp	Val	Glu	Ile	Ala	Pro	Glu
				260					265					270		
	Val	Gln	Ile	Glu	Ala	Asn	Val	Ile	Leu	Lys	Gly	Gln	Thr	Lys	Ile	Gly
25			275					280					285			
	Ala	Glu	Thr	Val	Leu	Thr	Asn	Gly	Thr	Tyr	Val	Val	Asp	Ser	Thr	Ile
		290					295					300				
30	Gly	Ala	Gly	Ala	Val	Ile	Thr	Asn	Ser	Met	Ile	Glu	Glu	Ser	Ser	Val
	305					310					315					320
	Ala	Asp	Gly	Val	Thr	Val	Gly	Pro	Tyr	Ala	His	Ile	Arg	Pro	Asn	Ser
					325					330					335	
35	Ser	Leu	Gly	Ala	Gln	Val	His	Ile	Gly	Asn	Phe	Val	Glu	Val	Lys	Gly
				340					345					350		
	Ser	Ser	Ile	Gly	Glu	Asn	Thr	Lys	Ala	Gly	His	Leu	Thr	Tyr	Ile	Gly
40			355					360					365			
	Asn	Cys	Glu	Val	Gly	Ser	Asn	Val	Asn	Phe	Gly	Ala	Gly	Thr	Ile	Thr
		370					375					380				
45	Val	Asn	Tyr	Asp	Gly	Lys	Asn	Lys	Tyr	Lys	Thr	Val	Ile	Gly	Val	Asn
	385					390					395					400
	Val	Phe	Val	Gly	Ser	Asn	Ser	Thr	Ile	Ile	Ala	Pro	Val	Glu	Leu	Gly
					405					410					415	
50	Asp	Asn	Ser	Leu	Val	Gly	Ala	Gly	Ser	Thr	Ile	Thr	Lys	Asp	Val	Pro
				420					425					430		
	Ala	Asp	Ala	Ile	Ala	Ile	Gly	Arg	Gly	Arg	Gln	Ile	Asn	Lys	Asp	Glu
55			435				440					445				
	Tyr	Ala	Thr	Arg	Leu	Pro	His	His	Pro	Lys	Asn	Gln				
		450					455					460				

<210> 196
 <211> 311
 5 <212> PRT
 <213> Streptococcus pneumoniae

<400> 196
 10 Met Ser Lys Ile Leu Val Phe Gly His Gln Asn Pro Asp Ser Asp Ala
 1 5 10 15
 Ile Gly Ser Ser Val Ala Phe Ala Tyr Leu Ala Lys Glu Ala Tyr Gly
 20 25 30
 15 Leu Asp Thr Glu Ala Val Ala Leu Gly Thr Pro Asn Glu Glu Thr Ala
 35 40 45
 Phe Val Leu Asn Tyr Phe Gly Val Glu Ala Pro Arg Val Ile Thr Ser
 50 55 60
 20 Ala Lys Ala Glu Gly Ala Glu Gln Val Ile Leu Thr Asp His Asn Glu
 65 70 75 80
 Phe Gln Gln Ser Val Ser Asp Ile Ala Glu Val Glu Val Tyr Gly Val
 85 90 95
 25 Val Asp His His Arg Val Ala Asn Phe Glu Thr Ala Ser Pro Leu Tyr
 100 105 110
 30 Met Arg Leu Glu Pro Val Gly Ser Ala Ser Ser Ile Val Tyr Arg Met
 115 120 125
 Phe Lys Glu His Gly Val Ala Val Pro Lys Glu Ile Ala Gly Leu Met
 130 135 140
 35 Leu Ser Gly Leu Ile Ser Asp Thr Leu Leu Leu Lys Ser Pro Thr Thr
 145 150 155 160
 40 His Pro Thr Asp Lys Ile Ile Ala Pro Glu Leu Ala Glu Leu Ala Gly
 165 170 175
 Val Asn Leu Glu Glu Tyr Gly Leu Ala Met Leu Lys Ala Gly Thr Asn
 180 185 190
 45 Leu Ala Ser Lys Ser Ala Glu Glu Leu Ile Asp Ile Asp Ala Lys Thr
 195 200 205
 Phe Glu Leu Asn Gly Asn Asn Val Arg Val Ala Gln Val Asn Thr Val
 210 215 220
 50 Asp Ile Ala Glu Val Leu Glu Arg Gln Ala Glu Ile Glu Ala Ala Met
 225 230 235 240
 55 Gln Ala Ala Asn Glu Ser Asn Gly Tyr Ser Asp Phe Val Leu Met Ile
 245 250 255
 Thr Asp Ile Val Asn Ser Asn Ser Glu Ile Leu Ala Leu Gly Ala Asn

260 265 270
 Met Asp Lys Val Glu Ala Ala Phe Asn Phe Lys Leu Glu Asn Asn His
 275 280 285
 5 Ala Phe Leu Ala Gly Ala Val Ser Arg Lys Lys Gln Val Val Pro Gln
 290 295 300
 Leu Thr Glu Ser Phe Asn Thr
 10 305 310
 <210> 197
 <211> 225
 15 <212> PRT
 <213> Streptococcus pneumoniae
 <400> 197
 20 Met Ile Ser Lys Arg Leu Glu Leu Val Ala Ser Phe Val Ser Gln Gly
 1 5 10 15
 Ala Ile Leu Leu Asp Val Gly Ser Asp His Ala Tyr Leu Pro Ile Glu
 20 25 30
 25 Leu Val Glu Arg Gly Gln Ile Lys Ser Ala Ile Ala Gly Glu Val Val
 35 40 45
 Glu Gly Pro Tyr Gln Ser Ala Val Lys Asn Val Glu Ala His Gly Leu
 50 55 60
 30 Lys Glu Lys Ile Gln Val Arg Leu Ala Asn Gly Leu Ala Ala Phe Glu
 65 70 75 80
 Glu Thr Asp Gln Val Ser Val Ile Thr Ile Ala Gly Met Gly Gly Arg
 35 85 90 95
 Leu Ile Ala Arg Ile Leu Glu Glu Gly Leu Gly Lys Leu Ala Asn Val
 100 105 110
 40 Glu Arg Leu Ile Leu Gln Pro Asn Asn Arg Glu Asp Asp Leu Arg Ile
 115 120 125
 Trp Leu Gln Asp His Gly Phe Gln Ile Val Ala Glu Ser Ile Leu Glu
 130 135 140
 45 Glu Ala Gly Lys Phe Tyr Glu Ile Leu Val Val Glu Ala Gly Gln Met
 145 150 155 160
 Lys Leu Ser Ala Ser Asp Val Arg Phe Gly Pro Phe Leu Ser Lys Glu
 50 165 170 175
 Val Ser Pro Val Phe Val Gln Lys Trp Gln Lys Glu Ala Glu Lys Leu
 180 185 190
 55 Glu Phe Ala Leu Gly Gln Ile Pro Glu Lys Asn Leu Glu Glu Arg Gln
 195 200 205

Val Leu Val Asp Lys Ile Gln Ala Ile Lys Glu Val Leu His Val Ser
 210 215 220

5 Lys
 225

10 <210> 198
 <211> 161
 <212> PRT
 <213> Streptococcus pneumoniae

15 <400> 198
 Met Asn Leu Asn Asp Ile Lys Asp Leu Met Thr Gln Phe Asp Gln Ser
 1 5 10 15

Ser Leu Arg Glu Phe Ser Tyr Lys Asn Gly Thr Asp Glu Leu Gln Phe
 20 25 30

20 Ser Lys Asn Glu Ala Arg Pro Val Pro Glu Val Ala Thr Gln Val Ala
 35 40 45

Pro Ala Pro Val Leu Ala Thr Pro Ser Pro Val Ala Pro Thr Ser Ala
 50 55 60

25 Pro Ala Glu Thr Val Ala Glu Glu Val Pro Ala Pro Ala Glu Ala Ser
 65 70 75 80

30 Val Ala Ser Glu Gly Asn Leu Val Glu Ser Pro Leu Val Gly Val Val
 85 90 95

Tyr Leu Ala Ala Gly Pro Asp Lys Pro Ala Phe Val Thr Val Gly Asp
 100 105 110

35 Ser Val Lys Lys Gly Gln Thr Leu Val Ile Ile Glu Ala Met Lys Val
 115 120 125

Met Asn Glu Ile Pro Ala Pro Lys Asp Gly Val Val Thr Glu Ile Leu
 130 135 140

40 Val Ser Asn Glu Glu Met Val Glu Phe Gly Lys Gly Leu Val Arg Ile
 145 150 155 160

45 Lys

50 <210> 199
 <211> 411
 <212> PRT
 <213> Streptococcus pneumoniae

55 <400> 199
 Met Lys Leu Asn Arg Val Val Val Thr Gly Tyr Gly Val Thr Ser Pro
 1 5 10 15

Ile Gly Asn Thr Pro Glu Glu Phe Trp Asn Ser Leu Ala Thr Gly Lys

	20	25	30
5	Ile Gly Ile Gly Gly Ile Thr Lys Phe Asp His Ser Asp Phe Asp Val 35 40 45		
	His Asn Ala Ala Glu Ile Gln Asp Phe Pro Phe Asp Lys Tyr Phe Val 50 55 60		
10	Lys Lys Asp Thr Asn Arg Phe Asp Asn Tyr Ser Leu Tyr Ala Leu Tyr 65 70 75 80		
	Ala Ala Gln Glu Ala Val Asn His Ala Asn Leu Asp Val Glu Ala Leu 85 90 95		
15	Asn Arg Asp Arg Phe Gly Val Ile Val Ala Ser Gly Ile Gly Gly Ile 100 105 110		
	Lys Glu Ile Glu Asp Gln Val Leu Arg Leu His Glu Lys Gly Pro Lys 115 120 125		
20	Arg Val Lys Pro Met Thr Leu Pro Lys Ala Leu Pro Asn Met Ala Ser 130 135 140		
25	Gly Asn Val Ala Met Arg Phe Gly Ala Asn Gly Val Cys Lys Ser Ile 145 150 155 160		
	Asn Thr Ala Cys Ser Ser Ser Asn Asp Ala Ile Gly Asp Ala Phe Arg 165 170 175		
30	Ser Ile Lys Phe Gly Phe Gln Asp Val Met Leu Val Gly Gly Thr Glu 180 185 190		
	Ala Ser Ile Thr Pro Phe Ala Ile Ala Gly Phe Gln Ala Leu Thr Ala 195 200 205		
35	Leu Ser Thr Thr Glu Asp Pro Thr Arg Ala Ser Ile Pro Phe Asp Lys 210 215 220		
40	Asp Arg Asn Gly Phe Val Met Gly Glu Gly Ser Gly Met Leu Val Leu 225 230 235 240		
	Glu Ser Leu Glu His Ala Glu Lys Arg Gly Ala Thr Ile Leu Ala Glu 245 250 255		
45	Val Val Gly Tyr Gly Asn Thr Cys Asp Ala Tyr His Met Thr Ser Pro 260 265 270		
	His Pro Glu Gly Gln Gly Ala Ile Lys Ala Ile Lys Leu Ala Leu Glu 275 280 285		
50	Glu Ala Glu Ile Ser Pro Glu Gln Val Ala Tyr Val Asn Ala His Gly 290 295 300		
55	Thr Ser Thr Pro Ala Asn Glu Lys Gly Glu Ser Gly Ala Ile Val Ala 305 310 315 320		
	Val Leu Gly Lys Glu Val Pro Val Ser Ser Thr Lys Ser Phe Thr Gly		

325 330 335
 His Leu Leu Gly Ala Ala Gly Ala Val Glu Ala Ile Val Thr Ile Glu
 340 345 350
 5 Ala Met Arg His Asn Phe Val Pro Met Thr Ala Gly Thr Ser Glu Val
 355 360 365
 10 Ser Asp Tyr Ile Glu Ala Asn Val Val Tyr Gly Gln Gly Leu Glu Lys
 370 375 380
 Glu Ile Pro Tyr Ala Ile Ser Asn Thr Phe Gly Phe Gly Gly His Asn
 385 390 395 400
 15 Ala Val Leu Ala Phe Lys Arg Trp Glu Asn Arg
 405 410
 20 <210> 200
 <211> 359
 <212> PRT
 <213> Streptococcus pneumoniae
 <400> 200
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 Leu Gly Glu Leu Leu Ser Asp Pro Asp Val Val Ser Asp Thr Lys Arg
 20 25 30
 30 Phe Met Glu Leu Ser Lys Glu Glu Ala Ser Asn Arg Asp Thr Val Ile
 35 40 45
 35 Ala Tyr Arg Glu Tyr Lys Gln Val Leu Gln Asn Ile Val Asp Ala Glu
 50 55 60
 Glu Met Ile Lys Glu Ser Gly Gly Asp Ala Asp Leu Glu Glu Leu Ala
 65 70 75 80
 40 Lys Gln Glu Leu Lys Asp Ala Lys Ala Glu Lys Glu Glu Tyr Glu Glu
 85 90 95
 Lys Leu Lys Ile Leu Leu Leu Pro Lys Asp Pro Asn Asp Asp Lys Asn
 100 105 110
 45 Ile Ile Leu Glu Ile Arg Gly Ala Ala Gly Gly Asp Glu Ala Ala Leu
 115 120 125
 Phe Ala Gly Asp Leu Leu Thr Met Tyr Gln Lys Tyr Ala Glu Ala Gln
 130 135 140
 50 Gly Trp Arg Phe Glu Val Met Glu Ala Ser Met Asn Gly Val Gly Gly
 145 150 155 160
 55 Phe Lys Glu Val Val Ala Met Val Ser Gly Gln Ser Val Tyr Ser Lys
 165 170 175

Leu Lys Tyr Glu Ser Gly Ala His Arg Val Gln Arg Val Pro Val Thr
 180 185 190
 5' Glu Ser Gln Gly Arg Val His Thr Ser Thr Ala Thr Val Leu Val Met
 195 200 205
 Pro Glu Val Glu Glu Val Glu Tyr Asp Ile Asp Pro Lys Asp Leu Arg
 210 215 220
 10 Val Asp Ile Tyr His Ala Ser Gly Ala Gly Gly Gln Asn Val Asn Lys
 225 230 235 240
 Val Ala Thr Ala Val Arg Ile Val His Leu Pro Thr Asn Ile Lys Val
 245 250 255
 15 Glu Met Gln Glu Glu Arg Thr Gln Gln Lys Asn Arg Glu Lys Ala Met
 260 265 270
 Lys Ile Ile Arg Ala Arg Val Ala Asp His Phe Ala Gln Ile Ala Gln
 275 280 285
 20 Asp Glu Gln Asp Ala Glu Arg Lys Ser Thr Ile Gly Thr Gly Asp Arg
 290 295 300
 25 Ser Glu Arg Ile Arg Thr Tyr Asn Phe Pro Gln Asn Arg Val Thr Asp
 305 310 315 320
 His Arg Ile Gly Leu Thr Leu Gln Lys Leu Asp Thr Ile Leu Ser Gly
 325 330 335
 30 Lys Leu Asp Glu Val Val Asp Ala Leu Val Leu Tyr Asp Gln Thr Gln
 340 345 350
 Lys Leu Glu Glu Leu Asn Lys
 35 355
 <210> 201
 <211> 559
 40 <212> PRT
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 Gly Leu Gly Glu Ile Gly Lys Asn Thr Tyr Gly Ile Glu Tyr Gln Asp
 20 25 30
 50 Glu Ile Ile Ile Val Asp Ala Gly Ile Lys Phe Pro Glu Asp Asp Leu
 35 40 45
 Leu Gly Ile Asp Tyr Val Ile Pro Asp Tyr Ser Tyr Ile Val Asp Asn
 50 55 60
 55 Ile Asp Arg Val Lys Ala Val Leu Ile Thr His Gly His Glu Asp His
 65 70 75 80

	Ile	Gly	Gly	Ile	Pro	Phe	Leu	Leu	Lys	Gln	Ala	Asn	Val	Pro	Ile	Tyr
					85					90					95	
5	Ala	Gly	Pro	Leu	Ala	Leu	Ala	Leu	Ile	Arg	Gly	Lys	Leu	Glu	Glu	His
				100					105					110		
	Gly	Leu	Leu	Arg	Asn	Ala	Lys	Leu	Tyr	Glu	Ile	Asn	His	Asn	Thr	Glu
			115					120					125			
10	Leu	Thr	Phe	Lys	Asn	Leu	Lys	Ala	Thr	Phe	Phe	Arg	Thr	Thr	His	Ser
		130					135					140				
	Ile	Pro	Glu	Pro	Leu	Gly	Ile	Val	Ile	His	Thr	Pro	Gln	Gly	Lys	Ile
15	145					150				155						160
	Val	Cys	Thr	Gly	Asp	Phe	Lys	Phe	Asp	Phe	Thr	Pro	Val	Gly	Glu	Pro
					165				170						175	
20	Ala	Asp	Leu	His	Arg	Met	Ala	Ala	Leu	Gly	Glu	Glu	Gly	Val	Leu	Cys
				180					185					190		
	Leu	Leu	Ser	Asp	Ser	Thr	Asn	Ala	Glu	Val	Pro	Thr	Phe	Thr	Asn	Ser
			195					200					205			
25	Glu	Lys	Val	Val	Gly	Gln	Ser	Ile	Met	Lys	Ile	Ile	Gln	Gly	Ile	Glu
		210					215					220				
	Gly	Arg	Ile	Ile	Phe	Ala	Ser	Phe	Ala	Ser	Asn	Ile	Phe	Arg	Leu	Gln
30	225					230					235					240
	Gln	Ala	Thr	Glu	Ala	Ala	Val	Lys	Thr	Gly	Arg	Lys	Ile	Ala	Val	Phe
					245					250					255	
35	Gly	Arg	Ser	Met	Glu	Lys	Ala	Ile	Val	Asn	Gly	Ile	Asp	Leu	Gly	Tyr
				260					265					270		
	Ile	Lys	Ala	Pro	Lys	Gly	Thr	Phe	Ile	Glu	Pro	Asn	Glu	Ile	Lys	Asp
			275					280					285			
40	Tyr	Pro	Ala	Gly	Glu	Val	Leu	Ile	Leu	Cys	Thr	Gly	Ser	Gln	Gly	Glu
		290					295					300				
	Pro	Met	Ala	Ala	Leu	Ser	Arg	Ile	Ala	Asn	Gly	Thr	His	Arg	Gln	Val
45	305					310					315					320
	Gln	Leu	Gln	Pro	Gly	Asp	Thr	Val	Ile	Phe	Ser	Ser	Ser	Pro	Ile	Pro
					325					330					335	
50	Gly	Asn	Thr	Thr	Ser	Val	Asn	Lys	Leu	Ile	Asn	Ile	Ile	Ser	Glu	Ala
				340					345					350		
	Gly	Val	Glu	Val	Ile	His	Gly	Lys	Val	Asn	Asn	Ile	His	Thr	Ser	Gly
			355					360					365			
55	His	Gly	Gly	Gln	Gln	Glu	Gln	Lys	Leu	Met	Leu	Cys	Leu	Ile	Lys	Pro
		370					375					380				

Lys Tyr Phe Met Pro Val His Gly Glu Tyr Arg Met Gln Lys Val His
 385 390 395 400
 5 Ala Gly Leu Ala Val Asp Thr Gly Val Glu Lys Asp Asn Ile Phe Ile
 405 410 415
 Met Ser Asn Gly Asp Val Leu Ala Leu Thr Ala Asp Ser Ala Arg Ile
 420 425 430
 10 Ala Gly His Phe Asn Ala Gln Asp Ile Tyr Val Asp Gly Asn Arg Ile
 435 440 445
 Gly Glu Ile Gly Ala Ala Val Leu Lys Asp Arg Arg Asp Leu Ser Glu
 450 455 460
 Asp Gly Val Val Leu Ala Val Ala Thr Val Asp Phe Lys Ser Gln Met
 465 470 475 480
 20 Ile Leu Ser Gly Pro Asp Ile Leu Ser Arg Gly Phe Val Tyr Met Arg
 485 490 495
 Glu Ser Gly Asp Leu Ile Arg Gln Ser Gln Arg Ile Leu Phe Asn Ala
 500 505 510
 25 Ile Arg Ile Ala Leu Lys Asn Lys Asp Ala Ser Val Gln Ser Val Asn
 515 520 525
 Gly Ala Ile Val Asn Ala Ile Arg Pro Phe Leu Tyr Glu Asn Thr Glu
 530 535 540
 Arg Glu Pro Ile Ile Ile Pro Met Ile Leu Thr Pro Asp Glu Glu
 545 550 555
 35
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 <211> 450
 <212> PRT
 <213> Streptococcus pneumoniae
 40
 <400> 202
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 45 Glu Gln Ser Val Leu Gly Ala Ile Phe Ile Asp Glu Ser Lys Leu Val
 20 25 30
 Phe Val Arg Glu Tyr Ile Glu Ser Arg Asp Phe Phe Lys Tyr Ala His
 35 40 45
 50 Arg Leu Ile Phe Gln Ala Met Val Asp Leu Ser Asp Arg Gly Asp Ala
 50 55 60
 55 Ile Asp Ala Thr Thr Val Arg Thr Ile Leu Asp Asn Gln Gly Asp Leu
 65 70 75 80
 Gln Asn Ile Gly Gly Leu Ser Tyr Leu Val Glu Ile Val Asn Ser Val

	85	90	95
5	Pro Thr Ser Ala Asn Ala Glu Tyr Tyr Ala Lys Ile Val Ala Glu Lys 100 105 110		
	Ala Met Leu Arg Arg Leu Ile Ala Lys Leu Thr Glu Ser Val Asn Gln 115 120 125		
10	Ala Tyr Glu Ala Ser Gln Pro Ala Asp Glu Ile Ile Ala Gln Ala Glu 130 135 140		
	Lys Gly Leu Ile Asp Val Ser Glu Asn Ala Asn Arg Ser Gly Phe Lys 145 150 155 160		
15	Asn Ile Arg Asp Val Leu Asn Leu Asn Phe Gly Asn Leu Glu Ala Arg 165 170 175		
20	Ser Gln Gln Thr Thr Asp Ile Thr Gly Ile Ala Thr Gly Tyr Arg Asp 180 185 190		
	Leu Asp His Met Thr Thr Gly Leu His Glu Glu Glu Leu Ile Ile Leu 195 200 205		
25	Ala Ala Arg Pro Ala Val Gly Lys Thr Ala Phe Ala Leu Asn Ile Ala 210 215 220		
	Gln Asn Ile Gly Thr Lys Leu Asp Lys Thr Val Ala Ile Phe Ser Leu 225 230 235 240		
30	Glu Met Gly Ala Glu Ser Leu Val Asp Arg Met Leu Ala Ala Glu Gly 245 250 255		
35	Leu Val Glu Ser His Ser Ile Arg Thr Gly Gln Leu Thr Asp Glu Glu 260 265 270		
	Trp Gln Lys Tyr Thr Ile Ala Gln Gly Asn Leu Ala Asn Ala Ser Ile 275 280 285		
40	Tyr Ile Asp Asp Thr Pro Gly Ile Arg Ile Thr Glu Ile Arg Ser Arg 290 295 300		
	Ser Arg Lys Leu Ala Gln Glu Thr Gly Asn Leu Gly Leu Ile Val Ile 305 310 315 320		
45	Asp Tyr Leu Gln Leu Ile Thr Gly Thr Gly Arg Glu Asn Arg Gln Gln 325 330 335		
50	Glu Val Ser Glu Ile Ser Arg Gln Leu Lys Ile Leu Ala Lys Glu Leu 340 345 350		
	Lys Val Pro Val Ile Ala Leu Ser Gln Leu Ser Arg Gly Val Glu Gln 355 360 365		
55	Arg Gln Asp Lys Arg Pro Val Leu Ser Asp Ile Arg Glu Ser Gly Ser 370 375 380		
	Ile Glu Gln Asp Ala Asp Ile Val Ala Phe Leu Tyr Arg Asp Asp Tyr		

150

	Ile	Asn	Ala	Phe	Gln	Pro	Glu	Glu	Tyr	Trp	Thr	Val	Asp	Ala	Val	Phe
			195					200					205			
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	Lys	Lys	Met	Lys	Leu	Thr	Ser	Asn	Asn	Glu	Val	Lys	Glu	Val	Leu	Ser
		225				230					235					240
10	Arg	Leu	Thr	Ser	Lys	Asp	Phe	Ser	Val	Asp	Gln	Val	Asp	Lys	Lys	Glu
					245					250					255	
	Arg	Lys	Arg	Asn	Ala	Pro	Leu	Pro	Tyr	Thr	Thr	Ser	Ser	Met	Gln	Met
15				260					265					270		
	Asp	Ala	Ala	Asn	Lys	Ile	Asn	Phe	Arg	Thr	Arg	Lys	Thr	Met	Met	Val
			275					280					285			
20	Ala	Gln	Gln	Leu	Tyr	Glu	Gly	Ile	Asn	Ile	Gly	Ser	Gly	Val	Gln	Gly
		290					295					300				
	Leu	Ile	Thr	Tyr	Met	Arg	Thr	Asp	Ser	Thr	Arg	Ile	Ser	Pro	Val	Ala
		305				310					315					320
25	Gln	Asn	Glu	Ala	Ala	Ser	Phe	Ile	Thr	Asp	Arg	Phe	Gly	Ser	Lys	Tyr
					325					330					335	
	Ser	Lys	His	Gly	Ser	Lys	Val	Lys	Asn	Ala	Ser	Gly	Ala	Gln	Asp	Ala
30				340					345					350		
	His	Glu	Ala	Ile	Arg	Pro	Ser	Ser	Val	Phe	Asn	Thr	Pro	Glu	Ser	Ile
			355					360					365			
35	Ala	Lys	Tyr	Leu	Asp	Lys	Asp	Gln	Leu	Lys	Leu	Tyr	Thr	Leu	Ile	Trp
		370					375					380				
	Asn	Arg	Phe	Val	Ala	Ser	Gln	Met	Thr	Ala	Ala	Val	Phe	Asp	Thr	Met
		385				390					395					400
40	Ala	Val	Lys	Leu	Ser	Gln	Lys	Gly	Val	Gln	Phe	Ala	Ala	Asn	Gly	Ser
					405					410					415	
	Gln	Val	Lys	Phe	Asp	Gly	Tyr	Leu	Ala	Ile	Tyr	Asn	Asp	Ser	Asp	Lys
45				420					425					430		
	Asn	Lys	Met	Leu	Pro	Asp	Met	Val	Val	Gly	Asp	Val	Val	Lys	Gln	Val
			435					440					445			
50	Asn	Ser	Lys	Pro	Glu	Gln	His	Phe	Thr	Gln	Pro	Pro	Ala	Arg	Tyr	Ser
		450					455					460				
	Glu	Ala	Thr	Leu	Ile	Lys	Thr	Leu	Glu	Glu	Asn	Gly	Val	Gly	Arg	Pro
		465				470					475					480
55	Ser	Thr	Tyr	Ala	Pro	Thr	Ile	Glu	Thr	Ile	Gln	Lys	Arg	Tyr	Tyr	Val
					485					490					495	

Arg Leu Ala Ala Lys Arg Phe Glu Pro Thr Glu Leu Gly Glu Ile Val
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 5 sn Lys Leu Ile Val Glu Tyr Phe Pro Asp Ile Val Asn Val Thr Phe
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 530 535 540
 10 Gln Trp Arg Arg Val Ile Asp Ala Phe Tyr Lys Pro Phe Ser Lys Glu
 545 550 555 560
 15 Val Ala Lys Ala Glu Glu Glu Met Glu Lys Ile Gln Ile Lys Asp Glu
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 580 585 590
 20 Leu Gly Arg Phe Gly Lys Phe Tyr Ala Cys Ser Asn Phe Pro Asp Cys
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 610 615 620
 25 Cys His Gln Gly Gln Ile Ile Glu Arg Lys Thr Lys Arg Asn Arg Leu
 625 630 635 640
 30 Phe Tyr Gly Cys Asn Arg Tyr Pro Glu Cys Glu Phe Thr Ser Trp Asp
 645 650 655
 Lys Pro Val Gly Arg Asp Cys Pro Lys Cys Gly Asn Phe Leu Met Glu
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 Gly Gln Gln Met His Glu Asp Val Lys Gln His Gln Ala Lys Ala Gly
 35 40 45
 55 Thr Pro Thr Met Gly Gly Leu Val Phe Leu Ile Thr Ser Val Leu Val

	50		55		60											
	Ala	Phe	Phe	Phe	Ala	Leu	Phe	Ser	Ser	Gln	Phe	Ser	Asn	Asn	Val	Gly
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5	Met	Ile	Leu	Phe	Ile	Leu	Val	Leu	Tyr	Gly	Leu	Val	Gly	Phe	Leu	Asp
					85					90					95	
	Asp	Phe	Leu	Lys	Val	Phe	Arg	Lys	Ile	Asn	Glu	Gly	Leu	Asn	Pro	Lys
10				100					105					110		
	Gln	Lys	Leu	Ala	Leu	Gln	Leu	Leu	Gly	Gly	Val	Ile	Phe	Tyr	Leu	Phe
			115					120					125			
15	Tyr	Glu	Arg	Gly	Gly	Asp	Met	Leu	Ser	Val	Phe	Gly	Tyr	Gln	Val	His
	130						135					140				
	Leu	Gly	Ile	Phe	Tyr	Ile	Val	Phe	Ala	Leu	Phe	Trp	Leu	Val	Gly	Phe
20	145					150					155					160
	Ser	Asn	Ala	Val	Asn	Leu	Thr	Asp	Gly	Val	Asp	Gly	Leu	Ala	Ser	Ile
					165					170					175	
	Ser	Val	Val	Ile	Ser	Leu	Ser	Ala	Tyr	Gly	Val	Ile	Ala	Tyr	Val	Gln
25				180					185					190		
	Gly	Gln	Met	Asp	Ile	Leu	Leu	Val	Ile	Leu	Ala	Met	Ile	Gly	Gly	Leu
			195					200					205			
30	Leu	Ser	Phe	Phe	Ile	Phe	Asn	His	Lys	Pro	Ala	Lys	Ile	Phe	Met	Gly
	210						215					220				
	Asp	Val	Gly	Ser	Leu	Ala	Leu	Gly	Gly	Met	Leu	Ala	Ala	Ile	Ser	Met
35	225					230				235						240
	Ala	Leu	His	Gln	Glu	Trp	Thr	Leu	Leu	Ile	Ile	Gly	Ile	Val	Tyr	Val
					245					250					255	
	Phe	Glu	Thr	Thr	Ser	Val	Met	Met	Gln	Val	Ser	Tyr	Phe	Lys	Leu	Thr
40				260					265					270		
	Gly	Gly	Lys	Arg	Ile	Phe	Arg	Met	Thr	Pro	Val	His	His	His	Phe	Glu
			275					280				285				
45	Leu	Gly	Gly	Leu	Ser	Gly	Lys	Gly	Asn	Pro	Trp	Ser	Glu	Trp	Lys	Val
	290						295					300				
	Asp	Phe	Phe	Phe	Trp	Gly	Val	Gly	Leu	Leu	Ala	Ser	Leu	Leu	Thr	Leu
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	Ala	Ile	Leu	Tyr	Leu	Met										
					325											
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	<212>	PRT														

<213> Streptococcus pneumoniae

<400> 205

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	Ala	His	Val	Asp	Ala	Gly	Lys	Thr	Thr	Thr	Thr	Glu	Arg	Ile	Leu	Tyr	20	25	30	
10	Tyr	Thr	Gly	Lys	Ile	His	Lys	Ile	Gly	Glu	Thr	His	Glu	Gly	Ala	Ser	35	40	45	
	Gln	Met	Asp	Trp	Met	Glu	Gln	Glu	Gln	Glu	Arg	Gly	Ile	Thr	Ile	Thr	50	55	60	
15	Ser	Ala	Ala	Thr	Thr	Ala	Gln	Trp	Asn	Asn	His	Arg	Val	Asn	Ile	Ile	65	70	75	80
20	Asp	Thr	Pro	Gly	His	Val	Asp	Phe	Thr	Ile	Glu	Val	Gln	Arg	Ser	Leu	85	90	95	
	Arg	Val	Leu	Asp	Gly	Ala	Val	Thr	Val	Leu	Asp	Ser	Gln	Ser	Gly	Val	100	105	110	
25	Glu	Pro	Gln	Thr	Glu	Thr	Val	Trp	Arg	Gln	Ala	Thr	Glu	Tyr	Gly	Val	115	120	125	
	Pro	Arg	Ile	Val	Phe	Ala	Asn	Lys	Met	Asp	Lys	Ile	Gly	Ala	Asp	Phe	130	135	140	
30	Leu	Tyr	Ser	Val	Ser	Thr	Leu	His	Asp	Arg	Leu	Gln	Ala	Asn	Ala	His	145	150	155	160
35	Pro	Ile	Gln	Leu	Pro	Ile	Gly	Ser	Glu	Asp	Asp	Phe	Arg	Gly	Ile	Ile	165	170	175	
	Asp	Leu	Ile	Lys	Met	Lys	Ala	Glu	Ile	Tyr	Thr	Asn	Asp	Leu	Gly	Thr	180	185	190	
40	Asp	Ile	Leu	Glu	Glu	Asp	Ile	Pro	Ala	Glu	Tyr	Leu	Asp	Gln	Ala	Gln	195	200	205	
	Glu	Tyr	Arg	Glu	Lys	Leu	Ile	Glu	Ala	Val	Ala	Glu	Thr	Asp	Glu	Glu	210	215	220	
45	Leu	Met	Met	Lys	Tyr	Leu	Glu	Gly	Glu	Glu	Ile	Thr	Asn	Glu	Glu	Leu	225	230	235	240
50	Lys	Ala	Gly	Ile	Arg	Lys	Ala	Thr	Ile	Asn	Val	Glu	Phe	Phe	Pro	Val	245	250	255	
	Leu	Cys	Gly	Ser	Ala	Phe	Lys	Asn	Lys	Gly	Val	Gln	Leu	Met	Leu	Asp	260	265	270	
55	Ala	Val	Ile	Asp	Tyr	Leu	Pro	Ser	Pro	Leu	Asp	Ile	Pro	Ala	Ile	Lys	275	280	285	

	Gly	Ile	Asn	Pro	Asp	Thr	Asp	Ala	Glu	Glu	Ile	Arg	Pro	Ala	Ser	Asp	
	290						295					300					
5	Glu	Glu	Pro	Phe	Ala	Ala	Leu	Ala	Phe	Lys	Ile	Met	Thr	Asp	Pro	Phe	
	305					310					315					320	
	Val	Gly	Arg	Leu	Thr	Phe	Phe	Arg	Val	Tyr	Ser	Gly	Val	Leu	Gln	Ser	
					325					330					335		
10	Gly	Ser	Tyr	Val	Leu	Asn	Thr	Ser	Lys	Gly	Lys	Arg	Glu	Arg	Ile	Gly	
				340					345					350			
	Arg	Ile	Leu	Gln	Met	His	Ala	Asn	Ser	Arg	Gln	Glu	Ile	Asp	Thr	Val	
			355					360					365				
15	Tyr	Ser	Gly	Asp	Ile	Ala	Ala	Ala	Val	Gly	Leu	Lys	Asp	Thr	Thr	Thr	
	370						375					380					
20	Gly	Asp	Ser	Leu	Thr	Asp	Glu	Lys	Ala	Lys	Ile	Ile	Leu	Glu	Ser	Ile	
	385					390					395					400	
	Asn	Val	Pro	Glu	Pro	Val	Ile	Gln	Leu	Met	Val	Glu	Pro	Lys	Ser	Lys	
					405					410					415		
25	Ala	Asp	Gln	Asp	Lys	Met	Gly	Ile	Ala	Leu	Gln	Lys	Leu	Ala	Glu	Glu	
				420					425					430			
	Asp	Pro	Thr	Phe	Arg	Val	Glu	Thr	Asn	Val	Glu	Thr	Gly	Glu	Thr	Val	
			435					440					445				
30	Ile	Ser	Gly	Met	Gly	Glu	Leu	His	Leu	Asp	Val	Leu	Val	Asp	Arg	Met	
	450						455					460					
35	Arg	Arg	Glu	Phe	Lys	Val	Glu	Ala	Asn	Val	Gly	Ala	Pro	Gln	Val	Ser	
	465					470					475					480	
	Tyr	Arg	Glu	Thr	Phe	Arg	Ala	Ser	Thr	Gln	Ala	Arg	Gly	Phe	Phe	Lys	
					485					490					495		
40	Arg	Gln	Ser	Gly	Gly	Lys	Gly	Gln	Phe	Gly	Asp	Val	Trp	Ile	Glu	Phe	
				500					505					510			
	Thr	Pro	Asn	Glu	Glu	Gly	Lys	Gly	Phe	Glu	Phe	Glu	Asn	Ala	Ile	Val	
			515					520					525				
45	Gly	Gly	Val	Val	Pro	Arg	Glu	Phe	Ile	Pro	Ala	Val	Glu	Lys	Gly	Leu	
	530						535					540					
50	Val	Glu	Ser	Met	Ala	Asn	Gly	Val	Leu	Ala	Gly	Tyr	Pro	Met	Val	Asp	
	545					550					555					560	
	Val	Lys	Ala	Lys	Leu	Tyr	Asp	Gly	Ser	Tyr	His	Asp	Val	Asp	Ser	Ser	
					565					570					575		
55	Glu	Thr	Ala	Phe	Lys	Ile	Ala	Ala	Ser	Leu	Ser	Leu	Lys	Glu	Ala	Ala	
				580					585					590			

Lys Ser Ala Gln Pro Ala Ile Leu Glu Pro Met Met Leu Val Thr Ile
 595 600 605
 5 Thr Val Pro Glu Glu Asn Leu Gly Asp Val Met Gly His Val Thr Ala
 610 615 620
 Arg Arg Gly Arg Val Asp Gly Met Glu Ala His Gly Asn Ser Gln Ile
 625 630 635 640
 10 Val Arg Ala Tyr Val Pro Leu Ala Glu Met Phe Gly Tyr Ala Thr Val
 645 650 655
 Leu Arg Ser Ala Ser Gln Gly Arg Gly Thr Phe Met Met Val Phe Asp
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 675 680 685
 20 Asn Lys Gly Glu Asp
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 35 40 45
 Thr Pro Lys Thr Val Cys Leu Asn Ser Ala Thr Ala Ala Leu Glu Leu
 50 55 60
 40 Ile Leu Arg Val Leu Glu Val Gly Pro Gly Asp Glu Val Ile Val Pro
 65 70 75 80
 Ala Met Thr Tyr Thr Ala Ser Cys Ser Val Ile Thr His Val Gly Ala
 85 90 95
 45 Thr Pro Val Met Val Asp Ile Gln Ala Asp Thr Phe Glu Met Asp Tyr
 100 105 110
 50 Asp Leu Leu Glu Gln Ala Ile Thr Glu Lys Thr Lys Val Ile Ile Pro
 115 120 125
 Val Glu Leu Ala Gly Ile Val Cys Asp Tyr Asp Arg Leu Phe Gln Val
 130 135 140
 55 Val Glu Lys Lys Arg Asp Phe Phe Thr Ala Ser Ser Lys Trp Gln Lys
 145 150 155 160

Ala Phe Asn Arg Ile Val Ile Val Ser Asp Ser Ala His Ala Leu Gly
 165 170 175
 5 Ser Thr Tyr Lys Gly Gln Pro Ser Gly Ser Ile Ala Asp Phe Thr Ser
 180 185 190
 Phe Ser Phe His Ala Val Lys Asn Phe Thr Thr Ala Glu Gly Gly Ser
 195 200 205
 10 Ala Thr Trp Lys Ala Asn Pro Val Ile Asp Asp Glu Glu Met Tyr Lys
 210 215 220
 Glu Phe Gln Ile Leu Ser Leu His Gly Gln Thr Lys Asp Ala Leu Ala
 15 225 230 235 240
 Lys Met Gln Leu Gly Ser Trp Glu Tyr Asp Ile Val Thr Pro Ala Tyr
 245 250 255
 20 Lys Cys Asn Met Thr Asp Ile Met Ala Ser Leu Gly Leu Val Gln Leu
 260 265 270
 Asp Arg Tyr Pro Ser Leu Leu Gln Arg Arg Lys Asp Ile Val Asp Arg
 275 280 285
 25 Tyr Asp Ser Gly Phe Ala Gly Ser Arg Ile His Pro Leu Ala His Lys
 290 295 300
 Thr Glu Thr Val Glu Ser Ser Arg His Leu Tyr Ile Thr Arg Val Glu
 30 305 310 315 320
 Gly Ala Ser Leu Glu Glu Arg Ser Leu Ile Ile Gln Glu Leu Ala Lys
 325 330 335
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 Ala Tyr Lys Asn Leu Gly Phe Asp Met Thr Asn Tyr Pro Lys Ala Tyr
 355 360 365
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				20					25					30		
5	Met	Glu	Glu	Leu	Gln	Asp	Glu	Val	Glu	Ile	Leu	Leu	Asp	Phe	Leu	Ala
			35					40					45			
	Glu	Asp	Glu	Ser	Val	His	Asp	Glu	Leu	Val	Ala	Gln	Leu	Ala	Glu	Leu
10		50					55					60				
	Asp	Lys	Ile	Met	Thr	Ser	Tyr	Glu	Met	Thr	Leu	Leu	Leu	Ser	Glu	Pro
	65					70					75					80
15	Tyr	Asp	His	Asn	Asn	Ala	Ile	Leu	Glu	Ile	His	Pro	Gly	Ser	Gly	Gly
					85					90					95	
	Thr	Glu	Ala	Gln	Asp	Trp	Gly	Asp	Met	Leu	Leu	Arg	Met	Tyr	Thr	Arg
				100					105					110		
20	Tyr	Gly	Asn	Ala	Lys	Gly	Phe	Lys	Val	Glu	Val	Leu	Asp	Tyr	Gln	Ala
			115					120					125			
	Gly	Asp	Glu	Ala	Gly	Ile	Lys	Ser	Val	Thr	Leu	Ser	Phe	Glu	Gly	Pro
25		130					135					140				
	Asn	Ala	Tyr	Gly	Leu	Leu	Lys	Ser	Glu	Met	Gly	Val	His	Arg	Leu	Val
	145					150					155					160
30	Arg	Ile	Ser	Pro	Phe	Asp	Ser	Ala	Lys	Arg	Arg	His	Thr	Ser	Phe	Thr
					165					170					175	
	Ser	Val	Glu	Val	Met	Pro	Glu	Leu	Asp	Asp	Thr	Ile	Glu	Val	Glu	Ile
				180					185					190		
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	225					230					235					240
45	Asn	Arg	Asp	Arg	Ala	Met	Lys	Met	Leu	Gln	Ala	Lys	Leu	Tyr	Gln	Met
					245					250					255	
	Glu	Gln	Glu	Lys	Lys	Ala	Ala	Glu	Val	Asp	Ser	Leu	Lys	Gly	Glu	Lys
				260					265					270		
50	Lys	Glu	Ile	Thr	Trp	Gly	Ser	Gln	Ile	Arg	Ser	Tyr	Val	Phe	Thr	Pro
			275					280					285			
	Tyr	Thr	Met	Val	Lys	Asp	His	Arg	Thr	Ser	Phe	Glu	Val	Ala	Gln	Val
55		290					295					300				
	Asp	Lys	Val	Met	Asp	Gly	Asp	Leu	Asp	Gly	Phe	Ile	Asp	Ala	Tyr	Leu

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 Val Tyr Met Ala Phe Ala Thr Lys Pro Lys Gln Phe Ile Phe Met Ala
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 25 Lys Lys Glu Leu Phe Thr Asn Arg Ile Phe Gly Trp Trp Ile Arg Met
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 Cys Gly Ala Phe Pro Ile Asp Arg Glu Asn Pro Ser Ala Ser Ala Ile
 85 90 95
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 100 105 110
 Phe Pro Ser Gly Ser Arg His Ser Asn Asp Val Lys Gly Gly Ala Ala
 115 120 125
 35 Leu Ile Ala Lys Met Ala Lys Val Arg Ile Met Pro Val Thr Tyr Thr
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 Asn Phe Gly Asn Pro Ile Asp Ile Ser Asp Ile Lys Lys Met Asn Asp
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 Leu Asp Glu Glu Thr Lys Gln Trp His Asn Asp Lys Lys Pro Asn Pro
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Pro Asp Lys Lys Arg Glu Glu Leu Ala
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Thr His Leu Ala Met Met Asp Ile Asp Asn Leu Tyr Gly Ala Phe Asp
35 40 45

20 Phe Leu Glu Ile Thr Lys Lys Tyr Gly Ile His Pro Leu Leu Gly Leu
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Glu Met Thr Val Phe Val Asp Asp Gln Gly Val Asn Leu Arg Phe Leu
65 70 75 80

25 Ala Leu Ser Ser Val Gly Tyr Gln Gln Leu Met Lys Leu Ser Thr Ala
85 90 95

30 Lys Met Gln Gly Glu Lys Thr Trp Ser Val Leu Ser Gln Tyr Leu Glu
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Asp Ile Ala Val Ile Val Pro Tyr Phe Asp Arg Val Glu Ser Leu Glu
115 120 125

35 Leu Gly Cys Asp Tyr Tyr Ile Gly Val Tyr Pro Glu Thr Leu Ala Ser
130 135 140

Glu Phe His His Pro Ile Leu Pro Leu Tyr Arg Val Asn Ala Phe Glu
145 150 155 160

40 Ser Arg Asp Arg Glu Val Leu Gln Val Leu Thr Ala Ile Lys Glu Asn
165 170 175

45 Leu Pro Leu Arg Glu Val Pro Leu Arg Ser Arg Gln Asp Val Phe Ile
180 185 190

Ser Ala Ser Ser Leu Glu Lys Leu Phe Gln Glu Arg Phe Pro Gln Ala
195 200 205

50 Leu Asp Asn Leu Glu Lys Leu Ile Ser Gly Ile Ser Tyr Asp Leu Asp
210 215 220

Thr Ser Leu Lys Leu Pro Arg Phe Asn Pro Ala Arg Pro Ala Val Glu
225 230 235 240

55 Glu Leu Arg Glu Arg Ala Glu Leu Gly Leu Val Gln Lys Gly Leu Thr
245 250 255

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5	Asp	Met	Gly	Phe	Asp	Asp	Tyr	Phe	Leu	Val	Val	Trp	Asp	Leu	Leu	Arg
			275					280					285			
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Thr Val Phe Glu Val Leu Lys
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	785					790					795					800	
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10	Asn Arg Leu Asp Phe Leu Asn Ser Gln Arg Asp Asp Ile Leu Ser Ala						
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	Lys Asn Leu Leu Leu Glu Thr Ile Thr Glu Met Asn Asp Glu Val Lys						
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	Thr Phe Lys Gln Met Phe Gly Gly Gly Gln Ala Asp Leu Ile Leu Thr						
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20	Glu Gly Asp Leu Leu Thr Ala Gly Val Glu Ile Ser Val Gln Pro Pro						
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	Gly Lys Lys Ile Gln Ser Leu Asn Leu Met Ser Gly Gly Glu Lys Ala						
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	Leu Ser Ala Leu Ala Leu Leu Phe Ser Ile Ile Arg Val Lys Thr Ile						
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	Val Lys Arg Phe Gly Asp Tyr Leu Asn Arg Phe Asp Lys Asp Ser Gln						
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	Ile Tyr Gly Val Thr Met Gln Glu Ser Gly Val Ser Lys Ile Val Ser						
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 <213> Streptococcus pneumoniae
 <400> 221
 30 Met Ser Glu Lys Leu Val Glu Ile Lys Asp Leu Glu Ile Ser Phe Gly
 1 5 10 15
 Glu Gly Ser Lys Lys Phe Val Ala Val Lys Asn Ala Asn Phe Phe Ile
 20 25 30
 35 Asn Lys Gly Glu Thr Phe Ser Leu Val Gly Glu Ser Gly Ser Gly Lys
 35 40 45
 Thr Thr Ile Gly Arg Ala Ile Ile Gly Leu Asn Asp Thr Ser Asn Gly
 50 55 60
 40 Asp Ile Ile Phe Asp Gly Gln Lys Ile Asn Gly Lys Lys Ser Arg Glu
 65 70 75 80
 45 Gln Ala Ala Glu Leu Ile Arg Arg Ile Gln Met Ile Phe Gln Asp Pro
 85 90 95
 Ala Ala Ser Leu Asn Glu Arg Ala Thr Val Asp Tyr Ile Ile Ser Glu
 100 105 110
 50 Gly Leu Tyr Asn His Arg Leu Phe Lys Asp Glu Glu Glu Arg Lys Glu
 115 120 125
 Lys Val Gln Asn Ile Ile Arg Glu Val Gly Leu Leu Ala Glu His Leu
 130 135 140
 55 Thr Arg Tyr Pro His Glu Phe Ser Gly Gly Gln Arg Gln Arg Ile Gly
 145 150 155 160

Ile Ala Arg Ala Leu Val Met Gln Pro Asp Phe Val Ile Ala Asp Glu
 165 170 175
 5 Pro Ile Ser Ala Leu Asp Val Ser Val Arg Ala Gln Val Leu Asn Leu
 180 185 190
 Leu Lys Lys Phe Gln Lys Glu Leu Gly Leu Thr Tyr Leu Phe Ile Ala
 195 200 205
 10 His Asp Leu Ser Val Val Arg Phe Ile Ser Asp Arg Ile Ala Val Ile
 210 215 220
 Tyr Lys Gly Val Ile Val Glu Val Ala Glu Thr Glu Glu Leu Phe Asn
 15 225 230 235 240
 Asn Pro Ile His Pro Tyr Thr Gln Ala Leu Leu Ser Ala Val Pro Ile
 245 250 255
 20 Pro Asp Pro Ile Leu Glu Arg Lys Lys Val Leu Lys Val Tyr Asp Pro
 260 265 270
 Ser Gln His Asp Tyr Glu Thr Asp Lys Pro Ser Met Val Glu Ile Arg
 275 280 285
 25 Pro Gly His Tyr Val Trp Ala Asn Gln Thr Glu Leu Ala Arg Tyr Gln
 290 295 300
 Lys Gly Leu Asn
 30 305
 <210> 222
 <211> 424
 35 <212> PRT
 <213> Streptococcus pneumoniae
 <400> 222
 Met Lys Ile Ser Trp Asn Gly Phe Ser Lys Lys Ser Tyr Gln Glu Arg
 40 1 5 10 15
 Leu Glu Leu Leu Lys Ala Gln Ala Leu Leu Ser Pro Glu Arg Gln Ala
 20 25 30
 45 Ser Leu Glu Lys Asp Glu Gln Met Ser Val Thr Val Ala Asp Gln Leu
 35 40 45
 Ser Glu Asn Val Val Gly Thr Phe Ser Leu Pro Tyr Ser Leu Val Pro
 50 50 55 60
 Glu Val Leu Val Asn Gly Gln Glu Tyr Thr Val Pro Tyr Val Thr Glu
 65 70 75 80
 Glu Pro Ser Val Val Ala Ala Ala Ser Tyr Ala Ser Lys Ile Ile Lys
 55 85 90 95
 Arg Ala Gly Gly Phe Thr Ala Gln Val His Gln Arg Gln Met Ile Gly

	100	105	110
	Gln Val Ala Leu Tyr Gln Ile Ala Asn Pro Lys Leu Ala Gln Glu Lys		
	115	120	125
5	Ile Ala Ser Lys Lys Ala Glu Leu Leu Glu Leu Ala Asn Gln Ala Tyr		
	130	135	140
	Pro Ser Ile Val Lys Arg Gly Gly Gly Ala Arg Asp Leu His Val Glu		
10	145	150	155
	Gln Ile Lys Gly Glu Pro Asp Phe Leu Val Val Tyr Ile His Val Asp		
	165	170	175
15	Thr Gln Glu Ala Met Gly Ala Asn Met Leu Asn Thr Met Leu Glu Ala		
	180	185	190
	Leu Lys Pro Val Leu Glu Glu Leu Ser Gln Gly Gln Ser Leu Met Gly		
20	195	200	205
	Ile Leu Ser Asn Tyr Ala Thr Asp Ser Leu Val Thr Ala Ser Cys Arg		
	210	215	220
	Ile Ala Phe Arg Tyr Leu Ser Arg Gln Lys Asp Gln Gly Arg Glu Ile		
25	225	230	235
	Ala Glu Lys Ile Ala Leu Ala Ser Gln Phe Ala Gln Ala Asp Pro Tyr		
	245	250	255
30	Arg Ala Ala Thr His Asn Lys Gly Ile Phe Asn Gly Ile Asp Ala Ile		
	260	265	270
	Leu Ile Ala Thr Gly Asn Asp Trp Arg Ala Ile Glu Ala Gly Ala His		
35	275	280	285
	Ala Phe Ala Ser Arg Asp Gly Arg Tyr Gln Gly Leu Ser Cys Trp Thr		
	290	295	300
	Leu Asp Leu Glu Arg Glu Glu Leu Val Gly Glu Met Thr Leu Pro Met		
40	305	310	315
	Pro Val Ala Thr Lys Gly Gly Ser Ile Gly Leu Asn Pro Arg Val Ala		
	325	330	335
45	Leu Ser His Asp Leu Leu Gly Asn Pro Ser Ala Arg Glu Leu Ala Gln		
	340	345	350
	Ile Ile Val Ser Ile Gly Leu Ala Gln Asn Phe Ala Ala Leu Lys Ala		
50	355	360	365
	Leu Val Ser Thr Gly Ile Gln Gln Gly His Met Lys Leu Gln Ala Lys		
	370	375	380
	Ser Leu Ala Leu Leu Ala Gly Ala Ser Glu Ser Glu Val Ala Pro Leu		
55	385	390	395
	Val Glu Arg Leu Ile Ser Asp Lys Thr Phe Asn Leu Glu Thr Ala Gln		

405 410 415
 Arg Tyr Leu Glu Asn Leu Arg Ser
 5 420
 <210> 223
 <211> 262
 <212> PRT
 10 <213> Streptococcus pneumoniae
 <400> 223
 Met Pro Ile Thr Ser Leu Glu Ile Lys Asp Lys Thr Phe Gly Thr Arg
 1 5 10 15
 15 Phe Arg Gly Phe Asp Pro Glu Glu Val Asp Glu Phe Leu Asp Ile Val
 20 25 30
 Val Arg Asp Tyr Glu Asp Leu Val Arg Ala Asn His Asp Lys Asn Leu
 35 40 45
 Arg Ile Lys Ser Leu Glu Glu Arg Leu Ser Tyr Phe Asp Glu Ile Lys
 50 55 60
 25 Asp Ser Leu Ser Gln Ser Val Leu Ile Ala Gln Asp Thr Ala Glu Arg
 65 70 75 80
 Val Lys Gln Ala Ala His Glu Arg Ser Asn Asn Ile Ile His Gln Ala
 85 90 95
 30 Glu Gln Asp Ala Gln Arg Leu Leu Glu Glu Ala Lys Tyr Lys Ala Asn
 100 105 110
 Glu Ile Leu Arg Gln Ala Thr Asp Asn Ala Lys Lys Val Ala Val Glu
 115 120 125
 35 Thr Glu Glu Leu Lys Asn Lys Ser Arg Val Phe His Gln Arg Leu Lys
 130 135 140
 40 Ser Thr Ile Glu Ser Gln Leu Ala Ile Val Glu Ser Ser Asp Trp Glu
 145 150 155 160
 Asp Ile Leu Arg Pro Thr Ala Thr Tyr Leu Gln Thr Ser Asp Glu Ala
 165 170 175
 45 Phe Lys Glu Val Val Ser Glu Val Leu Gly Glu Pro Ile Pro Ala Pro
 180 185 190
 Ile Glu Glu Glu Pro Ile Asp Met Thr Arg Gln Phe Ser Gln Ala Glu
 195 200 205
 50 Met Ala Glu Leu Gln Ala Arg Ile Glu Val Ala Asp Lys Glu Leu Ser
 210 215 220
 Glu Phe Glu Ala Gln Ile Lys Gln Glu Val Glu Ala Pro Thr Pro Val
 225 230 235 240

Val Ser Pro Gln Val Glu Glu Glu Pro Leu Leu Ile Gln Leu Ala Gln
 245 250 255

Cys Met Lys Asn Gln Lys
 260

<210> 224

<211> 575

<212> PRT

<213> Streptococcus pneumoniae

<400> 224

Met Ser Asn Gly Gln Leu Ile Tyr Leu Met Val Ala Ile Ala Val Ile
 1 5 10 15

Leu Val Leu Ala Tyr Val Val Ala Ile Phe Leu Arg Lys Arg Asn Glu
 20 25 30

Gly Arg Leu Glu Ala Leu Glu Glu Arg Lys Glu Glu Leu Tyr Asn Leu
 35 40 45

Pro Val Asn Asp Glu Val Glu Ala Val Lys Asn Met His Leu Ile Gly
 50 55 60

Gln Ser Gln Val Ala Phe Arg Glu Trp Asn Gln Lys Trp Val Asp Leu
 65 70 75 80

Ser Leu Asn Ser Phe Ala Asp Ile Glu Asn Asn Leu Phe Glu Ala Glu
 85 90 95

Gly Tyr Asn His Ser Phe Arg Phe Leu Lys Ala Ser His Gln Ile Asp
 100 105 110

Gln Ile Glu Ser Gln Ile Thr Leu Ile Glu Glu Asp Ile Ala Ala Ile
 115 120 125

Arg Asn Ala Leu Ala Asp Leu Glu Lys Gln Glu Ser Lys Asn Ser Gly
 130 135 140

Arg Val Leu His Ala Leu Asp Leu Phe Glu Glu Leu Gln His Arg Val
 145 150 155 160

Ala Glu Asn Ser Glu Gln Tyr Gly Gln Ala Leu Asp Glu Ile Glu Lys
 165 170 175

Gln Leu Glu Asn Ile Gln Ser Glu Phe Ser Gln Phe Val Thr Leu Asn
 180 185 190

Ser Ser Gly Asp Pro Val Glu Ala Ala Val Ile Leu Asp Asn Thr Glu
 195 200 205

Asn His Ile Leu Ala Leu Ser His Ile Val Asp Arg Val Pro Ala Leu
 210 215 220

Val Thr Thr Leu Ser Thr Glu Leu Pro Asp Gln Leu Gln Asp Leu Glu
 225 230 235 240

	Ala	Gly	Tyr	Arg	Lys	Leu	Ile	Asp	Ala	Asn	Tyr	His	Phe	Val	Glu	Thr	
					245					250					255		
5	Asp	Ile	Glu	Ala	Arg	Phe	His	Leu	Leu	Tyr	Glu	Ala	Phe	Lys	Lys	Asn	
				260					265					270			
	Gln	Glu	Asn	Ile	Arg	Gln	Leu	Glu	Leu	Asp	Asn	Ala	Glu	Tyr	Glu	Asn	
			275					280					285				
10	Gly	Gln	Ala	Gln	Glu	Glu	Ile	Asn	Ala	Leu	Tyr	Asp	Ile	Phe	Thr	Arg	
		290					295					300					
	Glu	Ile	Ala	Ala	Gln	Lys	Val	Val	Glu	Asn	Leu	Leu	Ala	Thr	Leu	Pro	
15	305					310					315					320	
	Thr	Tyr	Leu	Gln	His	Met	Lys	Glu	Asn	Asn	Thr	Leu	Leu	Gly	Glu	Asp	
					325					330					335		
20	Ile	Ala	Arg	Leu	Asn	Lys	Thr	Tyr	Leu	Leu	Pro	Glu	Thr	Ala	Ala	Ser	
				340					345					350			
	His	Val	Arg	Arg	Ile	Gln	Thr	Glu	Leu	Glu	Ser	Phe	Glu	Ala	Ala	Ile	
25			355					360					365				
	Val	Glu	Val	Thr	Ser	Asn	Gln	Glu	Glu	Pro	Thr	Gln	Ala	Tyr	Ser	Val	
		370					375					380					
30	Leu	Glu	Glu	Asn	Leu	Glu	Asp	Leu	Gln	Thr	Gln	Leu	Lys	Asp	Ile	Glu	
	385					390					395					400	
	Asp	Glu	Gln	Ile	Ser	Val	Ser	Glu	Arg	Leu	Thr	Gln	Ile	Glu	Lys	Asp	
					405					410					415		
35	Asp	Ile	Asn	Ala	Arg	Gln	Lys	Ala	Asn	Val	Tyr	Val	Asn	Arg	Leu	His	
				420					425					430			
	Thr	Ile	Lys	Arg	Tyr	Met	Glu	Lys	Arg	Asn	Leu	Pro	Gly	Ile	Pro	Gln	
			435					440					445				
40	Thr	Phe	Leu	Lys	Leu	Phe	Phe	Thr	Ala	Ser	Asn	Asn	Thr	Glu	Asp	Leu	
		450					455					460					
	Met	Val	Glu	Leu	Glu	Gln	Lys	Met	Ile	Asn	Ile	Glu	Ser	Val	Thr	Arg	
45	465					470					475					480	
	Val	Leu	Glu	Ile	Ala	Thr	Asn	Asp	Met	Glu	Ala	Leu	Glu	Thr	Glu	Thr	
					485					490					495		
50	Tyr	Asn	Ile	Val	Gln	Tyr	Ala	Thr	Leu	Thr	Glu	Gln	Leu	Leu	Gln	Tyr	
				500					505					510			
	Ser	Asn	Arg	Tyr	Arg	Ser	Phe	Asp	Glu	Arg	Ile	Gln	Glu	Ala	Phe	Asn	
			515					520					525				
55	Glu	Ala	Leu	Asp	Ile	Phe	Glu	Lys	Glu	Phe	Asp	Tyr	His	Ala	Ser	Phe	
		530					535					540					

Asp Lys Ile Ser Gln Ala Leu Glu Val Ala Glu Pro Gly Val Thr Asn
 545 550 555 560
 5 Arg Phe Val Thr Ser Tyr Glu Lys Thr Arg Glu Thr Ile Arg Phe
 565 570 575
 <210> 225
 <211> 800
 <212> PRT
 <213> Streptococcus pneumoniae
 <400> 225
 15 Met Leu Ile Ser Tyr Lys Trp Leu Lys Glu Leu Val Asp Ile Asp Val
 1 5 10 15
 Pro Ser Gln Glu Leu Ala Glu Lys Met Ser Thr Thr Gly Ile Glu Val
 20 20 25 30
 Glu Gly Val Glu Ser Pro Ala Ala Gly Leu Ser Lys Ile Val Val Gly
 35 40 45
 Glu Val Leu Ser Cys Glu Asp Val Pro Glu Thr His Leu His Val Cys
 25 50 55 60
 Gln Val Asn Val Gly Glu Glu Glu Arg Gln Ile Val Cys Gly Ala Pro
 65 70 75 80
 30 Asn Val Arg Ala Gly Ile Lys Val Met Val Ala Leu Pro Gly Ala Arg
 85 90 95
 Ile Ala Asp Asn Tyr Lys Ile Lys Lys Gly Lys Ile Arg Gly Leu Glu
 100 105 110
 35 Ser Leu Gly Met Ile Cys Ser Leu Gly Glu Leu Gly Ile Ser Asp Ser
 115 120 125
 Val Val Pro Lys Glu Phe Ala Asp Gly Ile Gln Ile Leu Pro Glu Asp
 40 130 135 140
 Ala Val Pro Gly Glu Glu Val Phe Ser Tyr Leu Asp Leu Asp Asp Glu
 145 150 155 160
 45 Ile Ile Glu Leu Ser Ile Thr Pro Asn Arg Ala Asp Ala Leu Ser Met
 165 170 175
 Cys Gly Val Ala His Glu Val Ala Ala Ile Tyr Asp Lys Ala Val Asn
 180 185 190
 50 Phe Lys Glu Phe Thr Leu Thr Glu Thr Asn Glu Ala Ala Ala Asp Ala
 195 200 205
 Leu Ser Val Ser Ile Glu Thr Asp Lys Ala Pro Tyr Tyr Ala Ala Arg
 55 210 215 220
 Ile Leu Asp Asn Val Thr Ile Ala Pro Ser Pro Gln Trp Leu Gln Asn

	225		230		235		240									
	Leu	Leu	Met	Asn	Glu	Gly	Ile	Arg	Pro	Ile	Asn	Asn	Val	Val	Asp	Val
					245					250					255	
5	Thr	Asn	Tyr	Ile	Leu	Leu	Tyr	Phe	Gly	Gln	Pro	Met	His	Ala	Phe	Asp
				260					265					270		
10	Leu	Asp	Asn	Phe	Glu	Gly	Thr	Asp	Ile	Arg	Val	Arg	Glu	Ala	Arg	Ala
			275					280					285			
	Gly	Glu	Lys	Leu	Val	Thr	Leu	Asp	Gly	Glu	Glu	Arg	Asp	Leu	Asp	Val
		290					295					300				
15	Asn	Asp	Leu	Val	Ile	Thr	Val	Ala	Asp	Lys	Pro	Val	Ala	Leu	Ala	Gly
	305					310					315					320
	Val	Met	Gly	Gly	Gln	Ala	Thr	Glu	Ile	Ser	Glu	Lys	Ser	Ser	Arg	Val
					325					330					335	
20	Val	Leu	Glu	Ala	Ala	Val	Phe	Asn	Gly	Lys	Ser	Ile	Arg	Lys	Thr	Ser
				340					345					350		
25	Gly	Arg	Leu	Asn	Leu	Arg	Ser	Glu	Ser	Ser	Ser	Arg	Phe	Glu	Lys	Gly
			355					360					365			
	Ile	Asn	Val	Ala	Thr	Val	Asn	Glu	Ala	Leu	Asp	Ala	Ala	Ala	Ser	Leu
		370					375				380					
30	Ile	Ala	Glu	Leu	Ala	Gly	Ala	Thr	Val	Arg	Lys	Gly	Ile	Val	Ser	Ala
	385					390					395					400
	Gly	Glu	Leu	Asp	Thr	Ser	Asp	Val	Glu	Val	Ser	Ser	Thr	Leu	Ala	Asp
				405						410					415	
35	Val	Asn	Arg	Val	Leu	Gly	Thr	Glu	Leu	Ser	Tyr	Ala	Asp	Val	Glu	Asp
				420					425					430		
40	Val	Phe	Arg	Arg	Leu	Gly	Phe	Gly	Leu	Ser	Gly	Asn	Ala	Asp	Ser	Phe
			435					440					445			
	Thr	Val	Arg	Val	Pro	Arg	Arg	Arg	Trp	Asp	Ile	Thr	Ile	Glu	Ala	Asp
		450					455					460				
45	Leu	Phe	Glu	Glu	Ile	Ala	Arg	Ile	Tyr	Gly	Tyr	Asp	Arg	Leu	Pro	Thr
	465					470					475					480
	Ser	Leu	Pro	Lys	Asp	Asp	Gly	Thr	Ala	Gly	Glu	Leu	Thr	Ala	Thr	Gln
				485						490					495	
50	Lys	Leu	Arg	Arg	Gln	Val	Arg	Thr	Ile	Ala	Glu	Gly	Ala	Gly	Leu	Thr
				500					505					510		
55	Glu	Ile	Ile	Thr	Tyr	Thr	Leu	Thr	Thr	Pro	Glu	Lys	Ala	Val	Glu	Phe
		515						520					525			
	Thr	Ala	Gln	Pro	Ser	Asn	Leu	Thr	Glu	Leu	Met	Trp	Pro	Met	Thr	Val

	530		535		540	
5	Asp Arg Ser Val Leu Arg Gln Asn Met Ile Ser Gly Ile Leu Asp Thr	545	550	555	560	
	Val Ala Tyr Asn Val Ala Arg Lys Asn Lys Asn Leu Ala Leu Tyr Glu	565	570		575	
10	Ile Gly Lys Val Phe Glu Gln Thr Gly Asn Pro Lys Glu Glu Leu Pro	580	585		590	
	Asn Glu Ile Asn Ser Phe Ala Phe Ala Leu Thr Gly Leu Val Ala Glu	595	600	605		
15	Lys Asp Phe Gln Thr Ala Ala Val Pro Val Asp Phe Phe Tyr Ala Lys	610	615	620		
20	Gly Ile Leu Glu Ala Leu Phe Thr Arg Leu Gly Leu Gln Val Thr Tyr	625	630	635	640	
	Thr Ala Thr Ser Glu Ile Ala Ser Leu His Pro Gly Arg Thr Ala Val	645	650		655	
25	Ile Ser Leu Gly Asp Gln Val Leu Gly Phe Leu Gly Gln Val His Pro	660	665		670	
	Val Thr Ala Lys Ala Tyr Asp Ile Pro Glu Thr Tyr Val Ala Glu Leu	675	680	685		
30	Asn Leu Ser Ala Ile Glu Ala Ala Leu Gln Pro Ala Thr Pro Phe Val	690	695	700		
35	Glu Ile Thr Lys Phe Pro Ala Val Ser Arg Asp Val Ala Leu Leu Leu	705	710	715	720	
	Lys Ala Glu Val Thr His Gln Glu Val Val Asp Ala Ile Gln Ala Ala	725	730		735	
40	Gly Val Lys Arg Leu Thr Asp Ile Lys Leu Phe Asp Val Phe Ser Gly	740	745	750		
	Glu Lys Leu Gly Leu Gly Met Lys Ser Met Ala Tyr Ser Leu Thr Phe	755	760	765		
45	Gln Asn Pro Glu Asp Ser Leu Thr Asp Glu Glu Val Ala Arg Tyr Met	770	775	780		
50	Glu Lys Ile Gln Ala Ser Leu Glu Glu Lys Val Asn Ala Glu Val Arg	785	790	795	800	
55	<210> 226					
	<211> 180					
	<212> PRT					

<213> Streptococcus pneumoniae

<400> 226

5 Met Leu Glu Asn Asp Ile Lys Lys Val Leu Val Ser His Asp Glu Ile
 1 5 10 15
 Thr Glu Ala Ala Lys Lys Leu Gly Ala Gln Leu Thr Lys Asp Tyr Ala
 20 25 30
 10 Gly Lys Asn Pro Ile Leu Val Gly Ile Leu Lys Gly Ser Ile Pro Phe
 35 40 45
 Met Ala Glu Leu Val Lys His Ile Asp Thr His Ile Glu Met Asp Phe
 50 55 60
 15 Met Met Val Ser Ser Tyr His Gly Gly Thr Ala Ser Ser Gly Val Ile
 65 70 75 80
 Asn Ile Lys Gln Asp Val Thr Gln Asp Ile Lys Gly Arg His Val Leu
 85 90 95
 Phe Val Glu Asp Ile Ile Asp Thr Gly Gln Thr Leu Lys Asn Leu Arg
 100 105 110
 25 Asp Met Phe Lys Ala Arg Glu Ala Ala Ser Val Lys Ile Ala Thr Leu
 115 120 125
 Leu Asp Lys Pro Glu Gly Arg Val Val Glu Ile Glu Ala Asp Tyr Thr
 130 135 140
 30 Cys Phe Thr Ile Pro Asn Glu Phe Val Val Gly Tyr Gly Leu Asp Tyr
 145 150 155 160
 Lys Glu Asn Tyr Arg Asn Leu Pro Tyr Ile Gly Val Leu Lys Glu Glu
 165 170 175
 Val Tyr Ser Asn
 180

40